GASTROINTESTINAL BLEEDING

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Gastrointestinal bleeding (GIB) is commonly encountered in clinical practice, in both outpatient and inpatient settings. Minor bleeding, such as from hemorrhoids, is exceedingly common. Major bleeding requiring a high level of care results in approximately 1 million hospital admissions in the United States every year.[1] Approximately 50% of these admissions are for upper gastrointestinal bleeding (UGIB), 40% for lower gastrointestinal bleeding (LGIB), and 10% for obscure GIB. Over the last 20 years, the widespread use of proton pump inhibitors (PPIs) has resulted in a decreased incidence of UGIB. However, mortality from UGIB has remained at 8 to 10% over the past 50 years. That mortality has failed to decrease substantially despite advances in patient care and technology may reflect the increasing number of elderly patients with comorbid illnesses. Acute GIB in individuals older than 60 accounts for 35 to 45% of all cases of acute UGIB but represents nearly all mortality associated with UGIB.[2–4]

GIB occurs when a pathologic process such as ulceration, inflammation, or neoplasia causes erosion of a blood vessel [*see Figure 1*]. The causes of GIB are protean and a reflection of the fact that many different kinds of lesions can bleed, many of which can be found in multiple locations in the gastrointestinal (GI) tract [*see Table 1*]. The size of the eroded vessel is an important determinant of the rate of bleeding, the risk of rebleeding, and the clinical outcome. The rate of blood loss is proportional to the diameter of the vessel; even small changes in vessel diameter have dramatic effects on bleeding rates. A study of the external diameter of arteries in gastric ulcers with recurrent bleeding revealed a range of 0.1 to 1.8 mm, with a mean of 0.7 mm.[5] Recurrent or persistent bleeding may result from inadequate vasoconstriction because of large vessel size, inflammatory necrosis of the vessel wall, pseudoaneurysm formation at the bleeding site, or systemic coagulopathies. See Table 2 for terms and definitions relating to GIB.

Acute Gastrointestinal Bleeding

INITIAL ASSESSMENT

When a patient presents with acute GIB, the initial steps should be to assess the patient's hemodynamic status and to ensure that there is clinical stability. Resuscitation is of the utmost importance if dictated by the clinical presentation. Next, the clinician must formulate an opinion about the severity of the bleeding and the site of bleeding. These clinical actions are all based on the history, the physical examination, and laboratory studies. Once this information is accumulated, the patient is then immediately triaged to the appropriate level of care (i.e., the hospital floor or monitored bed or intensive care unit [ICU]), and decisions about the urgency of endoscopy are made. A number of clinical factors have been used to assess prognosis in GIB [*see Table 3*].

History

History taking should be directed to answer the following questions: Does the patient have severe bleeding or is she or he at risk for severe bleeding? Is the bleeding from the upper or lower GI tract? What is the etiology?

Epigastric pain, nausea, hematemesis, and melena suggest UGIB, whereas hematochezia suggests LGIB. Hematochezia when associated with UGIB is usually accompanied by hemodynamic instability. Bleeding from a peptic ulcer should be suspected in patients taking aspirin or nonsteroidal antiinflammatory drugs (NSAIDs) or with a prior history of ulcer. Patients with heavy alcohol use or known or suspected cirrhosis may have variceal bleeding. Feeding tubes and a history of reflux or heavy alcohol use are risk factors for erosive esophagitis. Patients with surgical repair of abdominal aortic aneurysm can develop a fistula between the graft and the duodenum (although this is diminishingly small due to the nature of new grafts), and a high index of suspicion is needed for prompt management of this dangerous condition. Patients with a sudden, painless, large amount of hematochezia generally have diverticular bleeding. A history of radiation suggests radiation enteritis, colitis, or proctitis. Abdominal pain suggests peptic ulcer disease, inflammatory bowel disease, malignancy, or mesenteric ischemia. Abdominal pain—especially periumbilical cramping and gaseous distention—may be due to rapid intestinal transit of blood and suggests major bleeding. Chest pain, dizziness, and shortness of breath suggest severe blood loss and more urgent management. Similarly, patients on anticoagulants or antiplatelet drugs, with cirrhosis, or with a suspected aortoenteric fistula are at risk for severe bleeding and should be appropriately triaged.

Patients should be specifically asked about the use of aspirin, NSAIDs, antiplatelet agents, anticoagulants, iron pills, bismuth products (can change stool color to black), antacids, and acid-reducing medications. Many of the above medications are now available as over-the-counter drugs; hence, the patient may not volunteer that information, and they may not be included in the ambulatory medication list. A history of multiple blood transfusions should alert the physician to the possibility of antibodies (alloimmunization) and special requirements for ordering blood for transfusions.

Physical Examination

The vital signs are an integral part of the initial evaluation; it is especially important to detect signs of hypovolemia

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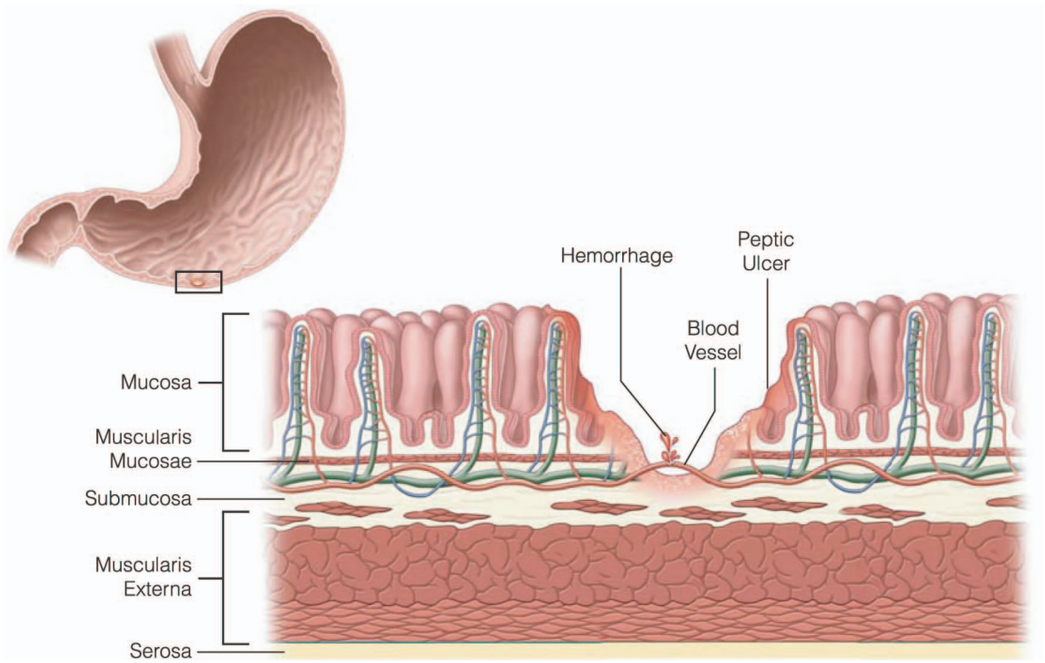

Figure 1 **Gastrointestinal bleeding occurs when a pathologic process causes erosion of the mucosa and exposes a submucosal blood vessel. A number of pathologic processes contribute to mucosal injury, for example, bacterial infection (*Helicobacter pylori* in the stomach), toxins (anywhere in the gastrointestinal tract), and aspirin or nonsteroidal inflammatory drugs (anywhere in the gastrointestinal tract).**

such as tachycardia, hypotension, and orthostasis. The pulmonary and cardiovascular examinations assess for medical comorbidities and are also needed for sedation assessment before endoscopy. The abdomen should be examined for tenderness, surgical scars, masses, and ascites. Skin examination can reveal pallor or signs of chronic liver disease such as spider angiomata, palmar erythema, caput medusa, or Dupuytren contracture. General examination can alert the clinician to the presence of chronic disease(s).

Table 1 Major Causes of Gastrointestinal Bleeding

Inflammatory
Peptic ulcer disease
Esophagitis or esophageal ulceration
Cameron erosions (diaphragmatic hernia)
Diverticular disease
Inflammatory bowel disease
Meckel diverticulum
Cancers and neoplasms
Primary lesion at any site
Metastatic deposits at any site
Large polyps
Gastrointestinal stromal tumors
Vascular anomalies
Gastroesophageal varices
Angiodysplasia
Dieulafoy lesion
Gastric antral vascular ectasia (watermelon stomach)
Radiation enteritis, colitis, and proctitis
Drugs
Aspirin
Nonsteroidal antiinflammatory drugs
Miscellaneous
Postpolypectomy
Mallory-Weiss tear

Laboratory Studies

The initial laboratory studies should include a complete blood count with differential and red blood cell indices, basic chemistries, liver enzymes, coagulation studies, and blood for typing and cross-screening/matching. The initial hematocrit value, if normal, should not necessarily suggest the absence of significant bleeding because it may take 24 to 72 hours for equilibration of intravascular red blood cells with extravascular fluid and hemodilution from intravenous (IV) administration of saline. A decrease of more than 2 g/dL indicates a significant bleeding episode. A mean corpuscular volume (MCV) less than 80 fL suggests iron deficiency anemia and possible chronic GI blood loss. An MCV less than 100 fL suggests chronic liver disease, alcoholism, or thiamine or folate deficiency. One important thing to remember is that if there is a suspicion of iron deficiency anemia, serum ferritin and iron studies should be performed before blood transfusion. An elevated white blood cell count can sometimes be observed in up to 50% of patients with severe GIB and does not necessarily indicate infection. A low platelet count, as in chronic liver disease, can contribute to the severity of bleeding. Blood urea nitrogen (BUN) may also be useful in patients with GIB; an elevated level may be due to hemoconcentration, chronic kidney disease, or GIB (increased intestinal urea absorption from breakdown of blood proteins). An increase in the ratio of BUN to creatinine to more than 25:1 strongly suggests an upper GI source. The

Table 2 Terms Relating to Gastrointestinal Bleeding and Their Definitions

Term	*Definition*
Obscure GIB	Source of bleeding not apparent after routine upper endoscopy, colonoscopy, and small bowel radiography
Occult GIB	Bleeding not clinically visible but can be detected directly by stool testing or suggested indirectly by iron deficiency anemia
Overt GIB	Visible red or altered blood noted in emesis or feces (i.e., hematemesis, melena, hematochezia)
Hematemesis	Includes vomiting of bright red blood (which suggests recent or ongoing bleeding) and dark material (coffee-ground emesis from altered blood, which suggests bleeding that stopped some time back)
Hematochezia	Passage of bright red blood per rectum usually indicating distal colonic or anorectal bleeding Brisk UGIB can result in hematochezia if accompanied by hemodynamic instability
LGIB	Bleeding from the colon or anorectum
Melena	Black, tarry stool resulting from degradation of blood to hematin by intestinal bacteria Bleeding from the upper GI tract, small bowel, or even proximal colon can result in melena Melena generally occurs after at least 50 to 100 cc of bleeding
Severe GIB	GIB accompanied by hemodynamic instability, a drop in hematocrit by at least 6%, or a drop in hemoglobin by at least 2 g/dL or appropriate transfusion of at least 2 units of packed red blood cells
UGIB	Bleeding from a source proximal to the ligament of Treitz (i.e., the esophagus, stomach, or duodenum)

GI = gastrointestinal; GIB = gastrointestinal bleeding; LGIB = lower gastrointestinal bleeding; UGIB = upper gastrointestinal bleeding.

coagulation studies, prothrombin time (PT), or international normalized ratio (INR) can be abnormal in patients with chronic liver disease or with the use of warfarin. Elevated liver tests, low albumin, and low platelets are biochemical clues to the presence of chronic liver disease.

An area of importance in patients with GIB has to do with the appropriate level of hematocrit after bleeding and/or prior to endoscopy. Limited data exist concerning the benefit of blood transfusion, particularly at modest levels of anemia (e.g., hematocrit 23 to 30%), although data in other areas, such as trauma, suggest that overly aggressive transfusion may be detrimental. Recent data concerning blood transfusion prior to endoscopy indicate that endoscopy is safe to perform even at very low hematocrits.[6] Ultimately, the decision to transfuse or not depends on individual factors in the context of excellent clinical judgment.

Table 3 Clinical High-Risk Criteria for Rebleeding and Mortality

Advanced age (≥ 70 yr)
Major organ comorbidities
In-hospital bleeding
Bright red hematemesis
Hypotension (systolic blood pressure < 100 mg Hg)
Tachycardia (heart rate > 100 beats/min)
Orthostasis (blood pressure drop > 20 mm Hg; heart rate rise > 20 beats/min)
Hemoglobin < 10 g/dL or drop of ≥ 2 g/dL
≥ 4 units of blood transfused in 24 hr

Some controversy also exists about to what degree to replace clotting factors and/or platelets in patients who are coagulopathic and/or thrombocytopenic, respectively. Limited data in this area also exist. However, common sense dictates that in situations with aggressive bleeding, attempts should be made to reverse such abnormalities. With regard to endoscopy in the setting of coagulopathy and bleeding, endoscopic therapy is critically important, and endoscopy need not be delayed while transfusing clotting factors and/or platelets.

Upper or Lower GIB?

Based on the history, physical examination, and laboratory studies, it is usually possible to distinguish between upper and lower GIB. Hematemesis, coffee-ground emesis, and melena usually indicate an upper GI source. Melena can be present when the bleeding source is in the small bowel or even the proximal colon. Red blood is observed with lower colonic or anorectal bleeding. In a small number of patients, bright red blood per rectum can be from brisk UGIB, particularly in the setting of hemodynamic instability. Maroon-colored stools are usually seen with small bowel or proximal colonic bleeding but, as mentioned above, can be seen with UGIB.

Nasogastric (NG) lavage may help distinguish between upper and lower GIB and assess the severity of bleeding. However, up to 25% of patients with UGIB can have a negative lavage. Bile in the NG lavage also makes UGIB unlikely but may be due to intermittent UGIB. Failure of NG lavage to clear with 500 cc of water generally indicates brisk UGIB and is an indication for urgent endoscopy. If a decision has already been taken to perform endoscopy, then NG lavage may be incremental in nature, although some endoscopists use it to aspirate the gastric contents and thus prevent the risk of aspiration during endoscopy. However, the pores in the NG tube are generally too small to suction blood and clots and hence may be ineffective.

Triage

On the basis of the history, the physical examination, laboratory studies, and possible NG lavage, the location (upper or lower) and severity of bleeding can usually be accurately assessed. This, along with age, medical comorbidities, and social factors, will dictate if the patient should be hospitalized or be scheduled for semiurgent endoscopy as an outpatient. If a patient needs hospitalization, then the next question is the level of care, that is, a regular bed versus the ICU. Although definite criteria for ICU admission may differ between institutions, patients in whom an ICU admission should be considered include those with the following: hypotension not responding with 2 L of IV fluids, variceal bleeding, clinically brisk bleeding in any setting and particularly in the setting of anticoagulation, and hematochezia

from an upper GI source. Other factors that may guide ICU admission include the need for endotracheal intubation for airway protection to prevent aspiration during endoscopy and hospital policies requiring emergent endoscopies to be performed in the ICU. Another reason for ICU admission is the high risk of recurrent GIB. This can be difficult to predict using clinical criteria, and early endoscopy (preferably in the emergency department or before hospital bed allocation) is now playing an increasingly important role in appropriate triage of patients with GIB. For example, patients with active bleeding, any stigmata of recent hemorrhage (visible vessel, protuberance at ulcer base), or a nondiagnostic study (e.g., a clot obscuring complete visualization) can be considered high risk and be admitted to a more monitored setting such as the ICU or the intermediate care unit. Patients with minor GI lesions such as a clean ulcer base, Mallory-Weiss (MW) tear (without bleeding), esophagitis, gastritis, duodenitis, or other benign findings can be discharged to home provided that other discharge criteria are fulfilled.

ENDOSCOPIC MANAGEMENT

A variety of endoscopic modalities are currently available for the management of GIB. These can be categorized as thermal, mechanical, and injection devices. These devices are available as long catheters that are passed through channels in the endoscope.

Thermal devices can generate heat directly or indirectly by passage of current through the tissue. They cause hemostasis by causing edema, coagulation of tissue protein, contraction of vessels, and indirect activation of the coagulation cascade, thereby resulting in a hemostatic bond. Thermal devices are either contact (i.e., the mucosa is touched with the device for hemostasis; examples are a heater probe and multipolar electrocautery) or noncontact (e.g., argon plasma coagulator). The contact thermal devices also allow coaptation of vessels, which may contribute to hemostasis [*see Figure 2*].

Injection therapy is usually performed using epinephrine (diluted 1:10,000 or 1:20,000) injected within 1 to 2 mm of the bleeding site. This therapy achieves hemostasis by creating tamponade and causes vessel constriction [*see Figure 3*]. The primary mechanism is tamponade, so a large amount of solution (15 to 20 cc) may need to be injected. This can result in up to a fivefold increase in the circulating plasma epinephrine level but, apart from transient tachycardia, rarely causes any clinically significant cardiovascular event. Injections with sclerosants such as alcohol or ethanolamine oleate are now used only as second-line therapy for variceal bleeding due to complications associated with tissue damage.

Mechanical devices are small hemostatic clips that are passed through the endosope and deployed over the bleeding site. They apply a clamping force that closes off the blood vessels therein [*see Figure 4*]. Depending on the site and size of bleeding, multiple clips may be needed. After a few days, the clips detach and fall off on their own. Hemoclips are sometimes preferred over thermal hemostasis in patients with coagulopathy because there is no tissue thermal damage, thereby mitigating the risk of delayed bleeding.

Band ligation is a technique in which mucosa is suctioned into a plastic cap (with mounted rubber bands) fitted at the end of the endoscope, and the band is rolled off the cap and over the lesion to pinch the suctioned mucosa at its base. This technique is classically used for the treatment of varices but can be used for other lesions in special situations.

SMALL BOWEL IMAGING

Endoscopic techniques for examination of the small bowel that are currently available include push enteroscopy, single-balloon enteroscopy (SBE), double-balloon enteroscopy (DBE), Spirus enteroscopy, intraoperative enteroscopy, and wireless capsule endoscopy (WCE). Except for WCE, the other techniques are traditional endoscopic techniques in the sense that they use endoscopes, the patient has to be sedated, and accessories can be passed through the endoscope, making it possible to take biopsies and perform other therapeutic maneuvers. They differ in the type of endoscope, overtube, technique, and length of small bowel that can be examined. Push enteroscopy was the first technique used for enteroscopy, but the extent of small bowel that could be visualized was limited due to looping of the endoscope in the stomach and the small bowel. The newer techniques of SBE, DBE, and Spirus enteroscopy, all forms of "deep enteroscopy," work by pleating the small intestine over the endoscope, effectively shortening the small bowel (like pleating a curtain over a rod). The enteroscopes can be inserted orally (antegrade approach) or rectally (retrograde approach). Complete examination of the small bowel can be performed, albeit rarely, using only the antegrade approach. The retrograde approach can then be used whereby the small bowel is visualized by passing the endoscope across the ileocecal valve into the ileum and then advancing it as far as possible. The overall diagnostic yield of deep enteroscopy is around 65%.[7] Intraoperative enteroscopy, performed during exploratory laparotomy through single or multiple enterotomy sites, is indicated for the occasional patient with active or recurrent major bleeding of obscure origin. Complications include mucosal laceration, intramural hematoma, mesenteric hemorrhage, and intestinal ischemia. Currently, Spirus enteroscopy overtubes are no longer being manufactured.

For WCE, the patient comes to the endoscopy unit and is given a small capsule (about 11 × 26 mm) to swallow [*see Figure 5*]. No sedation is required. The capsule, which is disposable, contains a color video chip, a light source, and a transmitter. As the capsule travels through the digestive tract by peristalsis, it takes two pictures per second. The images are transmitted to a data recorder, which is the size of a "Walkman" and is worn around the waist on a belt. The recorder stores images taken for 8 hours. At the end of the 8 hours, the patient returns the recorder, and the images can be loaded on to a computer and analyzed. The capsule takes approximately 50,000 images during its transit. The capsule eventually is expelled in the stool. This noninvasive technology provides images of the entire small bowel; however, it is purely a diagnostic modality. This technique may be beneficial in patients with recurrent or occult GIB of obscure origin, but it is not appropriate in hemodynamically unstable patients with major active bleeding. The diagnostic yield of capsule endoscopy in patients with obscure GIB ranges from 45 to 66%.

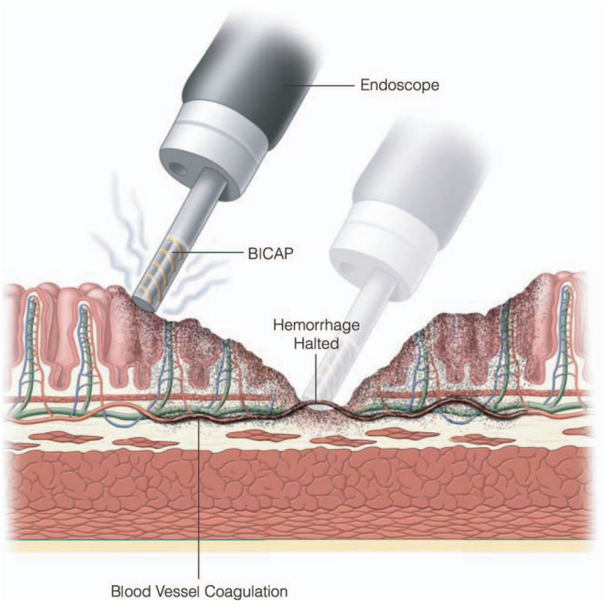

Figure 2 **Hemostasis of a bleeding ulcer with coagulation of the blood vessel with a bipolar probe. The probe is typically depressed in a tangential fashion around and on the bleeding vessel. BICAP = bipolar electrocoagulation.**

RADIOLOGIC IMAGING

Radionuclide Technetium Scan

A technetium-99m–labeled red blood cell scan is sometimes considered when active bleeding is suspected, but the results of endoscopy are negative. Nuclear scans can detect bleeding at rates that exceed 0.1 mL/min.[8] These scans have a reported false positive rate of about 22%, which is usually due to rapid transit of blood so that labeled blood is detected in the colon, although it originated from a more proximal source.[9] A positive result is more reliable when the scan is done early rather than delayed for several hours. The red blood cell scan poorly localizes the bleeding site, which becomes a problem during subsequent enteroscopy.

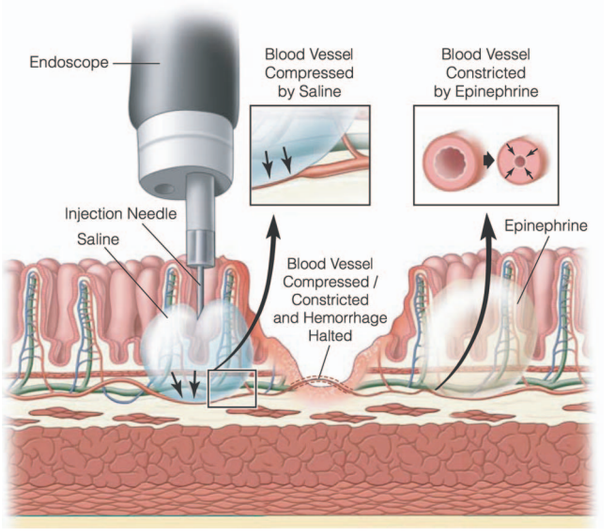

Figure 3 **Hemostasis of a bleeding ulcer with injection of saline or epinephrine, which compresses and/or constricts the blood vessel. Dilute epinephrine (1:10,000) is injected around the bleeding lesion; this leads to tamponade and/or constriction of feeding vessels and subsequent hemostasis.**

Angiography

Angiography is considered when endoscopic therapy for an established lesion has failed and surgery is not an option or when the site of active bleeding remains obscure after endoscopy. An optimal examination with a high positive yield is best obtained when there is active bleeding at rates exceeding 0.5 to 1 mL/min.[10] The possibility of therapeutic embolization of the bleeding vessel at the same time makes this technique especially useful [*see Figure 6*]. Significant complications—including contrast reaction, acute renal failure, and femoral artery thrombosis—have been reported in approximately 9% of cases.[11] The reported sensitivity of angiography varies from 22 to 87%. The specificity approaches 100%.[12]

Upper Gastrointestinal Bleeding

UGIB is arbitrarily defined as hemorrhage from a source proximal to the ligament of Treitz (i.e., the esophagus, stomach, or duodenum). Although this is the most accepted definition, it is interesting to note that the ligament of Treitz cannot be identified on imaging or endoscopically. Hematemesis essentially always reflects UGIB, and stools may range from black (melena) to bright red (hematochezia), depending on the rates of bleeding and intestinal transit. Initial management includes stabilization of hemodynamics, as highlighted above. The most critical decision surrounds the timing of endoscopy. Patients with evidence of active bleeding should undergo emergent endoscopy [*see Figure 7*], typically within minutes to hours. Patients with less aggressive bleeding can undergo expectant endoscopy. After cessation of active UGIB, patients may experience melena for 2 to 3 days. In and of itself, such melena is not necessarily an indication of rebleeding, especially if the patient's hemoglobin level does not decrease.

PEPTIC ULCER DISEASE

Peptic ulcer accounts for 50% of cases of UGIB and is the most common cause of UGIB in the United States. It is responsible for almost 100,000 hospitalizations every year.[3,13] Peptic ulcers are most commonly caused by aspirin or other NSAIDs, *Helicobacter pylori*, or both. *H. pylori* infection has a prevalence of 20 to 50% in developed countries.[14] It is implicated in both gastric and duodenal ulcers. The lifetime risk of peptic ulcer disease from *H. pylori* infection ranges from 3% in the United States to 25% in Japan. Due to better detection and treatment of *H. pylori*, the proportion of ulcers caused by NSAIDs has increased.[15]

NSAIDs are widely used, and in the United States, more than 30 billion NSAID tablets are consumed annually. Except for sodium salicylate, all NSAIDs can cause bleeding. Acetaminophen is not associated with GIB. NSAIDs

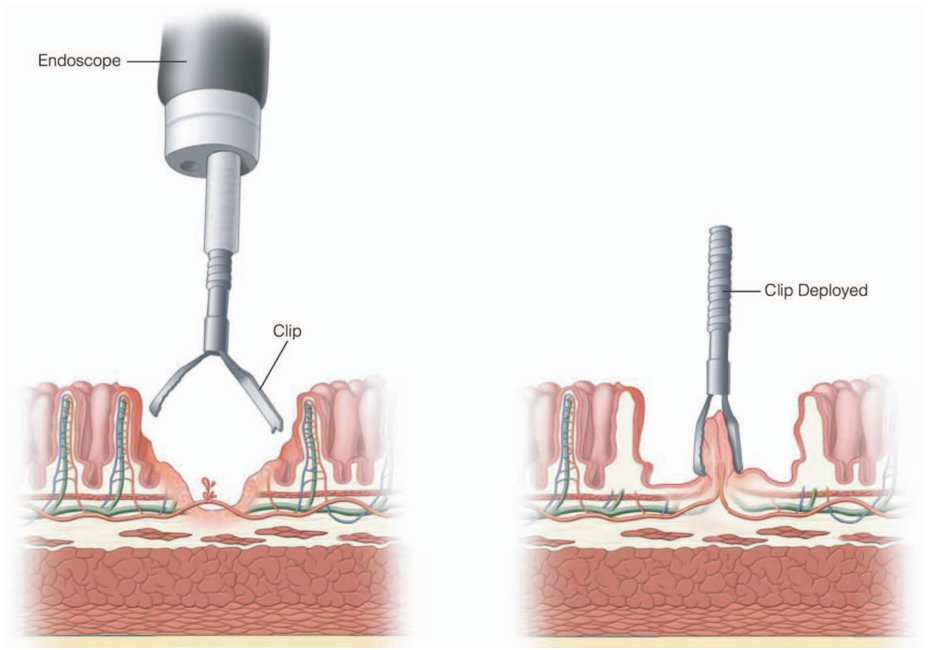

Figure 4 **Hemostasis of a bleeding ulcer with a mechanical clip. The clip is applied in such a fashion that it physically compresses feeding and/or index blood vessels.**

cause ulceration by inhibiting the cyclooxygenase-mediated synthesis of prostaglandins, which play a key role in maintaining gastric mucosal integrity. NSAIDs are more likely to cause gastric ulcers than duodenal ulcers. Gastroduodenal ulcers may be observed in 15 to 45% of patients who have taken NSAIDs regularly.[16] Elderly individuals are especially susceptible to NSAID-induced GIB.[17] Use of selective serotonin reuptake inhibitors (SSRIs) is associated with a higher risk of UGIB, especially in patients who are also taking NSAIDs or low-dose aspirin.[18] Anticoagulants and nonaspirin antiplatelet drugs do not cause GIB per se, but they can unmask or aggravate hemorrhage from preexisting lesions.

Endoscopic Management

The endoscopic appearance of the ulcer is helpful in selecting endoscopic treatment, triaging, and duration of hospital stay. Forrest in 1974 described rebleeding rates of an ulcer based on endoscopic stigmata of recent hemorrhage [*see Figure 8 and Figure 9*].[19] This concept has now been extended to also predict risk of rebleeding after endoscopic therapy [*see Table 4*].[20,21] The location of the ulcer is also a predictive factor for recurrent GIB.

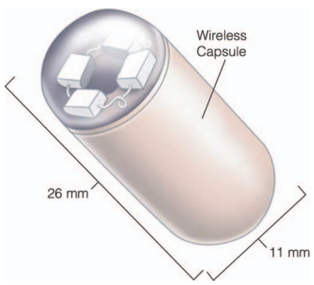

Figure 5 **Wireless capsule. The capsule, which contains a sophisticated miniature camera and a transmitter device, is swallowed and passes through the gastrointestinal tract. Signals from the capsule are recorded electronically and viewed at a viewing station.**

Medical Management

Initial drug therapy for major nonvariceal UGIB is directed at gastric acid suppression, and PPIs are the cornerstone of medical management [*see Figure 7*]. IV PPIs are commonly used during hospitalizations, but it is important to know which patients actually benefit from their use because IV PPIs are expensive and their use has been associated with nosocomial pneumonia. The rationale for using IV PPI is that it sufficiently raises gastric pH (pH > 6), which aids in clot stabilization.[22]

In the initial studies that demonstrated clear efficacy of IV PPIs for high-risk peptic ulcer bleeding, the drug was administered after endoscopic diagnosis and hemostasis.[23–25] Use of IV PPIs in patients with major stigmata of ulcer hemorrhage (active bleeding, nonbleeding visible vessel, or a clot) reduces the risk of rebleeding and the need for surgical intervention. Patients with endoscopic stigmata of oozing, a flat spot, or a clean ulcer base have a low risk of bleeding and do not need an IV PPI. Later studies were conducted in which IV PPIs were administered to patients in the emergency department prior to endoscopy.[26–28] These studies demonstrated that this approach reduced the likelihood of encountering high-risk lesions in need of endoscopic therapy. The advocates of this approach suggest that this decreases the length of hospitalization and the need for prolonged IV PPIs postendoscopy. However, all of these studies failed to demonstrate an effect on mortality, the number of transfusions, rebleeding, or the need for surgical intervention.

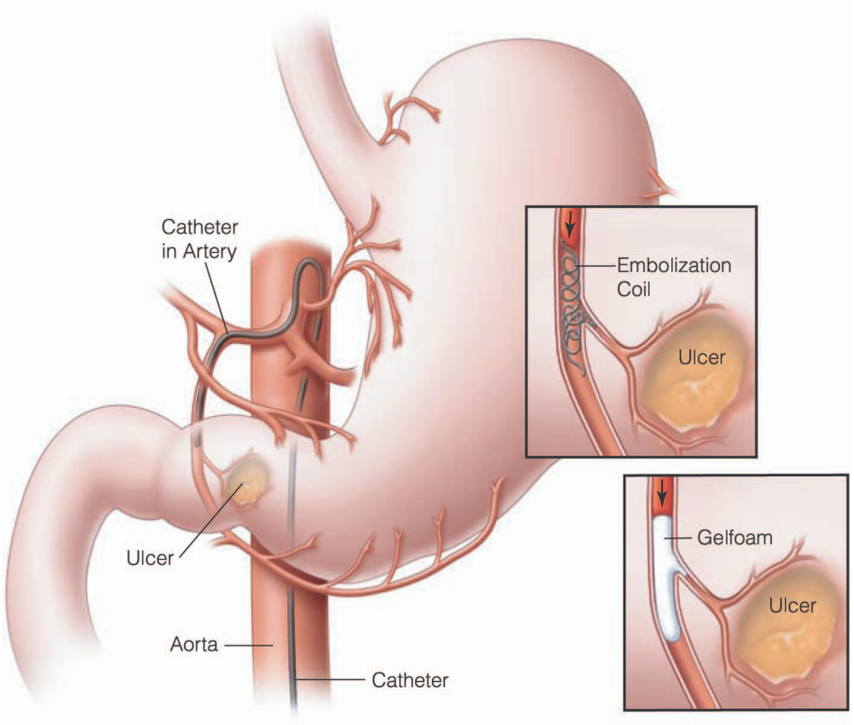

Figure 6 **Diagnosis of a bleeding vessel with angiography and hemostasis by coil embolization or insertion of Gelfoam. Embolization with either coils or Gelfoam causes injury, inflammation, and physical occlusion of the blood vessel, which leads to cessation of bleeding.**

IV PPIs are continued for 72 hours, and this practice stems from studies in which serial endoscopies were performed and it was seen that the risk of rebleeding decreases significantly after 72 hours.[29–31] The ulcers with minor stigmata of recent hemorrhage generally resolve over 2 to 4 days.[32]

Radiologic and Surgical Management

Patients who have recurrent bleeding despite two separate attempts at endoscopic hemostasis should be considered for management by interventional radiology. The technique involves first identifying the bleeding vessel by selectively cannulating the artery supplying the suspected bleeding site. Once the bleeding vessel is identified, it can be superselectively cannulated and embolized. The materials that have been used include occlusion devices (such as microcoils), an absorbable gelatin sponge, and tissue adhesives. The risks associated with embolization include misplacement of embolic material, inadvertent distal reflux of embolic agent, and excessive devascularization of an organ leading to ischemia and eventual luminal stenosis. A study of superselective embolization in 48 patients with LGIB showed that embolization was the definitive treatment in 44% of patients, with a 27% technical failure rate.[33,34] If embolization therapy does not control bleeding, then surgery remains an option. Surgery should be especially considered when a vessel greater than 2 mm in diameter is visible within the culprit lesion, the ulcer is located in the posterior duodenal bulb (this location is associated with the large gastroduodenal artery), or the patient has exsanguination and when patients cannot be medically resuscitated. However, overall rebleeding and mortality rates for angiography with embolization and surgery are comparable, and the final choice often depends on local availability and expertise.

VARICEAL BLEEDING

Gastroesophageal variceal bleeding, due to portal hypertension [*see Figure 10*], accounts for 10 to 30% of all upper GI hemorrhages. Gastroesophageal varices are identified in about 30% of patients with compensated cirrhosis and 60% patients with decompensated cirrhosis. Variceal bleeding occurs in 10 to 20% of cirrhotic patients per year.[35,36] Endoscopic intervention along with pharmacologic treatment achieves control of bleeding in nearly 70 to 80% of episodes of variceal bleeding.[37] Despite appropriate management, the mortality rate with each bleeding is about 30%, and long-term survival is less than 40% after patients present with overt major bleeding.[38,39] Variceal bleeding is distinctive, with large-volume hematemesis of bright red blood [*see Figure 11*] or clots, and is associated with severe hemodynamic instability. Approximately 75% of bleeding varices are esophageal in origin and 25% gastric in origin. Up to one third of initial variceal bleeding results in mortality. The most common site of bleeding is the distal 5 cm of the esophagus because of relatively greater variceal distention and thinner supporting tissue surrounding the veins in this region compared with the upper and the middle esophagus. Physicians should bear in mind that up to 50% of patients with portal hypertension have GIB that is unrelated to variceal bleeding. The long-term survival of these patients continues to be poor and is less than 40% after 1 year of medical treatment.

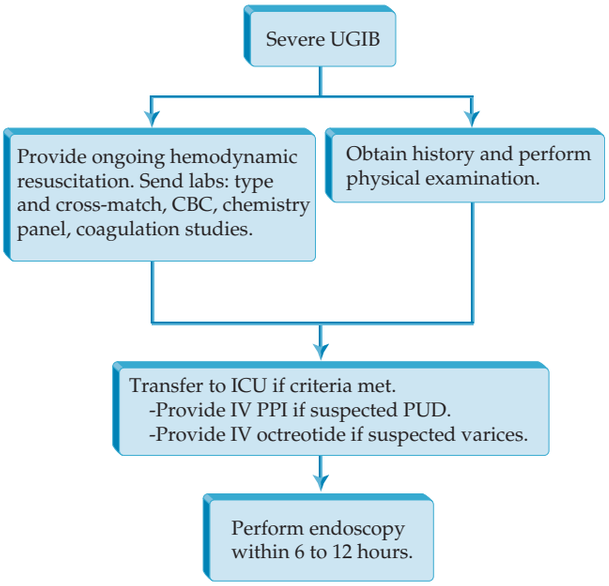

Figure 7 **Algorithm for upper gastrointestinal bleeding (UGIB). The decision regarding the timing of endoscopy should be made based on clinical grounds. In patients with aggressive bleeding and/or unstable hemodynamics, endoscopy should be performed emergently in the hope of identifying an actively bleeding lesion and stopping the bleeding. In patients in whom bleeding is not obviously active, the planning of endoscopy is often predicated on a variety of factors. Endoscopy is indicated within 24 hours but may occur early (i.e., within hours of presentation) or be slightly delayed (i.e., within 24 hours). Only in patients with other, active nongastrointestinal issues should endoscopy be delayed more than 24 hours. CBC = complete blood count; ICU = intensive care unit; IV = intravenous; PPI = proton pump inhibitor; PUD = peptic ulcer disease.**

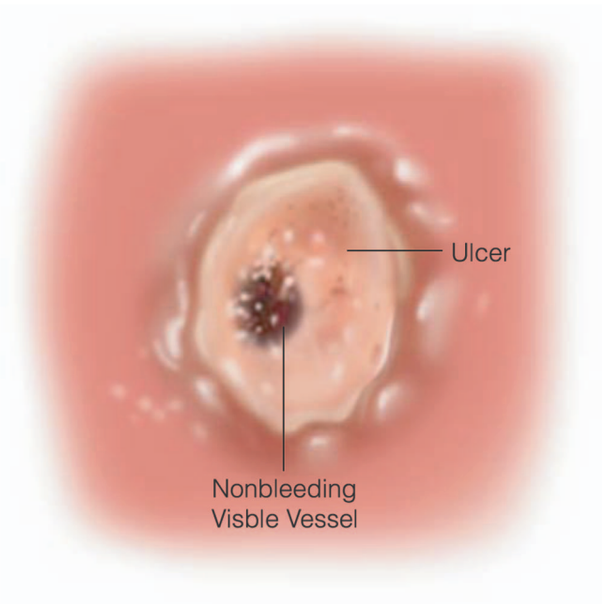

Figure 8 **Example of a high-risk duodenal bulbar ulcer. The ulcer contains a protuberant punctum, assigning it to a high-risk category. Such lesions may be treated with any of the means of therapy highlighted in Figure 2, Figure 3, and Figure 4. The current standard of care is to use dual-modality treatment, typically injection plus either coagulation or clip therapy.**

Medical Management

Somatostatin and its long acting analogue, octreotide, cause selective splanchnic vasoconstriction, thereby decreasing portal blood flow. Although these drugs are probably as effective as sclerotherapy in controlling acute variceal bleeding, they have not been shown to promote survival benefit. Somatostatin is reported to stop variceal bleeding in 80% of patients.[39,40] Octreotide is administered as a 50 µg bolus followed by continuous infusion at 50 µg/hr for 72 hours. Side effects are few and include hyperglycemia and abdominal pain. There are ongoing studies to determine if a shorter duration of octreotide is efficacious. The combination of octreotide and endoscopic therapy appears to offer better control of acute bleeding than either alone.

Other drugs include vasopressin, which is a potent vasoconstrictor and has a reported overall success rate of 50%. However, its use has fallen out of favor due to systemic vasoconstrictive side effects that may lead to myocardial or mesenteric ischemia with a high rebleeding rate when the medication is discontinued (likely due to a short half-life).[41] Terlipressin is a synthetic analogue of vasopressin that has fewer side effects and a longer half-life; it is given in bolus injections and is used outside the United States.

Bacterial infections are a frequent complication in patients with cirrhosis and UGIB and are observed in up to 22% of patients within 48 hours. Up to 66% of patients develop infections within 7 to 14 days. Bacterial infections are associated with an increased risk of rebleeding, which has a mortality rate of up to 50%. Oral antibiotics, active against enteric bacteria, have been commonly used as antibiotic prophylaxis in patients with cirrhosis and UGIB and improve survival.[42] The most commonly used antibiotics include oral norfloxacin 400 mg twice a day, IV ciprofloxacin 400 mg every 12 hours, IV levofloxacin 500 mg every 24 hours, and ceftriaxone 1 g every 24 hours. The antibiotics are usually given for 7 days. The role of beta blockers is primarily prophylactic. These agents are not used in the acute management of variceal bleeding.

Endoscopic Management

Endoscopic treatment is used primarily for esophageal variceal bleeding; the techniques include band ligation and sclerotherapy. At the time of endoscopy, the varices may be actively bleeding or have stigmata of recent bleeding such as a protruding vessel or visible vessel [*see Figure 8*]. Band ligation is considered the first-line endoscopic therapy for esophageal varices. Comparative studies report a better initial control of bleeding (91% versus 77%) and lower rebleeding rates (24% versus 47%) with band ligation than with sclerotherapy. Also, the band ligations have lower complication rates than sclerotherapy.[43–46]

Endoscopic band ligation involves placing rubber bands over a varix [*see Figure 1*2]. This blocks the blood flow across the varix, which subsequently undergoes thrombosis and fibrosis. Band ligation is as effective as sclerotherapy in

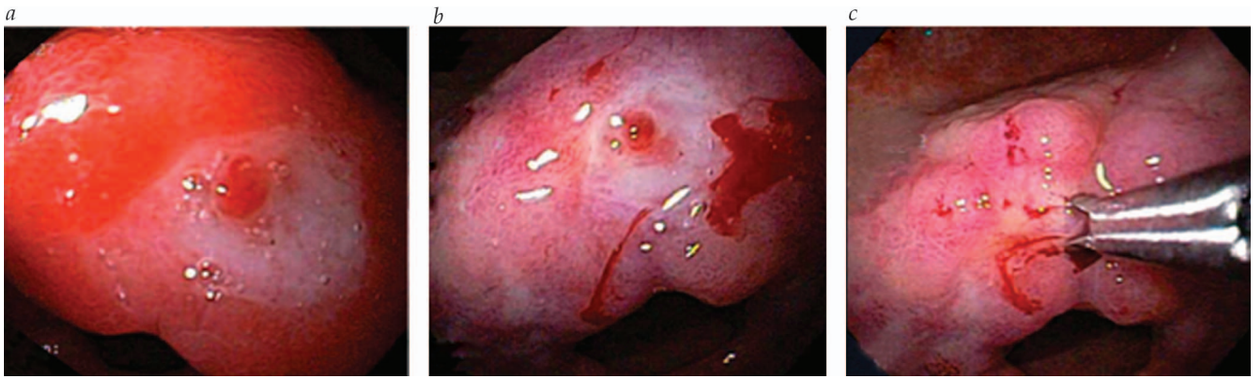

Figure 9 **Treatment of a high-risk gastric ulcer with a nonbleeding visible vessel. (*a*) An ulcer with a raised, red, hemorrhagic spot can be readily visualized. This lesion represents a nonbleeding visible vessel. (*b*) This image depicts the lesion after the periphery of the lesion was treated with epinephrine injections (the fresh blood shown to the right is typical of trivial bleeding after removal of the needle). The area surrounding the ulcer bed can be seen to be blanched a whitish color, consistent with a vasoconstrictive effect of epinephrine. (*c*) A hemoclip has been placed over the visible vessel while opposing the edges of the ulcer (this was possible given the small size of the ulcer but will not always be possible, particularly with larger ulcers).**

achieving initial hemostasis, requires fewer endoscopic treatment sessions, and has essentially replaced sclerotherapy as the preferred modality due to late complications of sclerotherapy.[44] The band ligation is repeated every 3 to 4 weeks until complete obliteration of varices is achieved. After obliteration, an upper endoscopy is repeated at 3 months and then annually thereafter because varices can recur. Complications of banding include retrosternal chest pain, dysphagia from compromise of the esophageal lumen, band ulceration (usually superficial ulcers that heal within 2 weeks), and esophageal perforation. Complication rates vary from 2 to 19%.[45,46]

Endoscopic sclerotherapy involves injecting a sclerosant into or adjacent to the varices [*see Figure 13*]. The commonly used sclerosants include ethanol and ethanolamine oleate. Transient activation of coagulation causes cessation of blood flow by thrombosis. This is followed by more permanent obliteration of varices by fibrosis. The initial activation of coagulation is the result of an acute inflammatory process provoked by oleate, and this explains the clinical manifestations as mild fever, retrosternal pain, leukocytosis, and an increase in plasma fibrinogen level observed after sclerotherapy. The complications of sclerotherapy, which have made it less attractive, include ulcers at the site of injection (which can later bleed), esophageal strictures, bleeding, perforation, fever, chest pain, and bacteremia. Solutions such as fibrin and cyanoacrylate glue are injected inside the blood vessel, where they quickly form a plug and seal the blood vessel.

Endoscopic glue injection with cyanoacrylates is now considered the first-line endoscopic intervention for bleeding gastric varices and secondary prevention of gastric variceal bleeding outside the United States. Initial hemostatic rates with this therapy are not yet approved by the Food and Drug Administration. Cyanoacrylates are synthetic glues that rapidly polymerize on contact with water or blood. Several case series have shown it be superior to sclerotherapy for bleeding gastric varices.[47–49]

If bleeding continues despite endoscopic therapy or if endoscopic therapy cannot be initiated, then a modified Sengstaken-Blakemore (Minnesota) tube should be inserted [*see Figure 14*]. However, this is only a temporary measure

Table 4 Endoscopic High-Risk Stigmata for Rebleeding and Indications for Endoscopic Therapy

Clinical Variable	*Frequency (%)*	*Rebleeding Risk (%)*	*Rebleeding Risk after Endoscopic Hemostasis (%)*	*Recommended Endoscopic Treatment*	*High-Dose Intravenous PPI*	*Admission*
Active bleeding	10	90	15–30	Dual therapy	Yes	ICU or intermediate unit
Visible vessel	20	50	15–30	Dual therapy	Yes	ICU or intermediate unit
Adherent clot	10	30	0–5	Remove clot then treat accordingly	Yes	24 hr observation
Oozing	15	15	0–5	Dual therapy	No	24 hr observation
Flat spot	10	0–5	0	Not necessary	No	Can be discharged
Clean-based ulcer	35	0–5	0	Not necessary	No	Can be discharged

Numbers are estimates based on the author's experience and body of published literature.
ICU = intensive care unit; PPI = proton pump inhibitor.

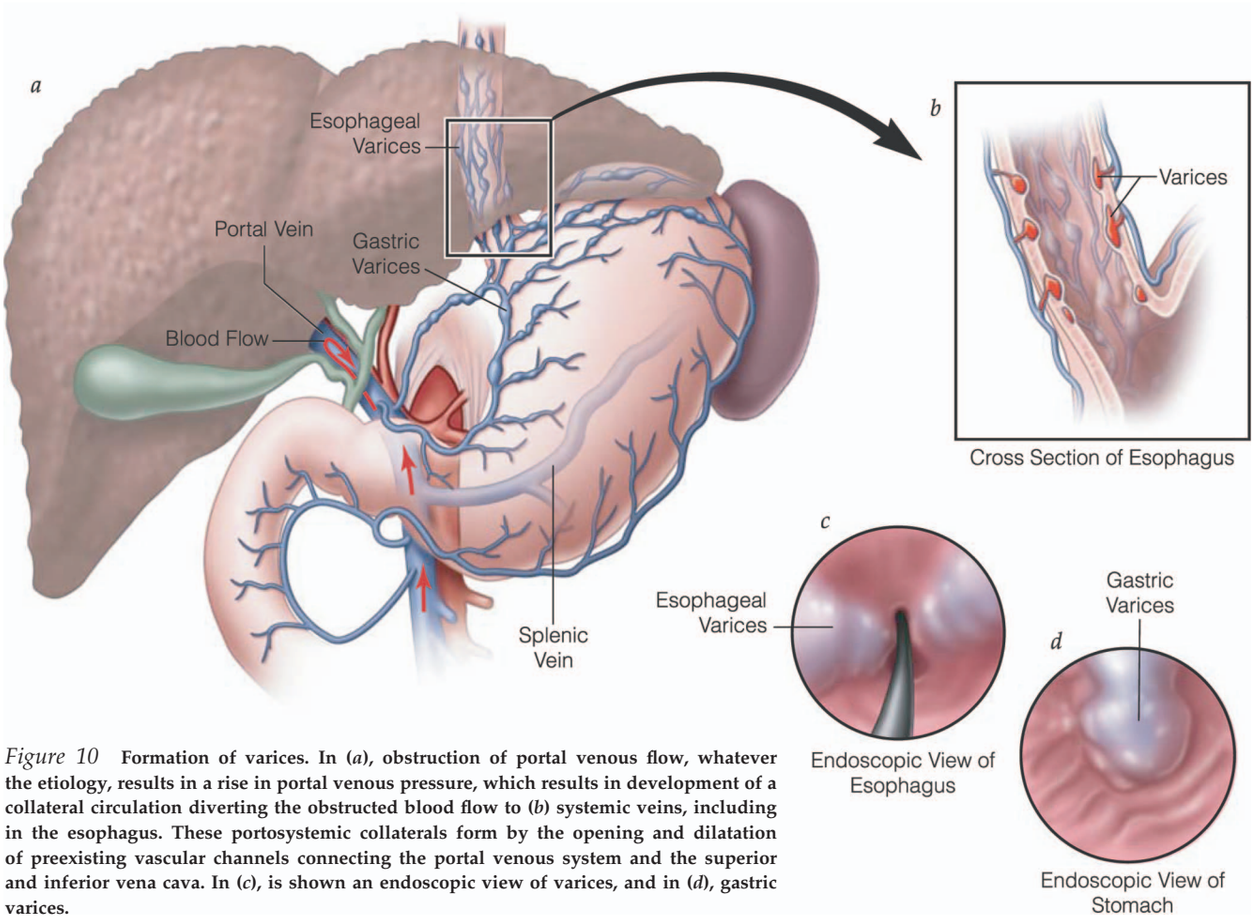

Figure 10 **Formation of varices. In (*a*), obstruction of portal venous flow, whatever the etiology, results in a rise in portal venous pressure, which results in development of a collateral circulation diverting the obstructed blood flow to (*b*) systemic veins, including in the esophagus. These portosystemic collaterals form by the opening and dilatation of preexisting vascular channels connecting the portal venous system and the superior and inferior vena cava. In (*c*), is shown an endoscopic view of varices, and in (*d*), gastric varices.**

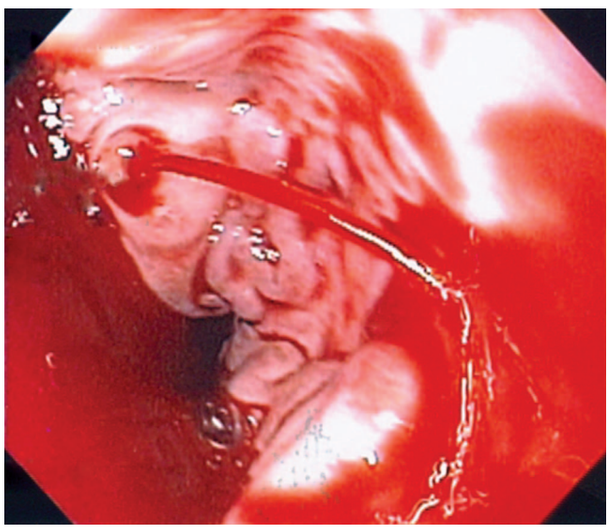

Figure 11 **Varices with a spurting lesion. A (nonpulsatile) stream of blood can be seen coming from a large varix in the distal esophagus.**

until more definitive treatment—endoscopic, radiologic, or surgical—can be undertaken.

Preventive measures may be indicated in patients with esophageal varices. Preventive measures are generally offered to patients who have a history of GIB and to those who have large esophageal varices without a previous bleeding event. Currently, the accepted preventive measures for variceal bleeding include endoscopic band ligation, beta-blocker therapy, or a combination of both. Ligation is performed every 14 to 21 days until varices are completely eradicated, which typically requires three or four sessions.

Radiologic intervention available for variceal bleeding involves the transjugular intrahepatic portosystemic shunt (TIPS). The procedure involves percutaneous insertion of a metal stent between the hepatic and portal veins, thereby creating a shunt between portal and systemic circulation. This decreases the pressure in the portal vein and esophageal and gastric varices. The accepted indications for TIPS are bleeding or rebleeding that cannot be controlled by either pharmacologic or endoscopic therapy. A recent study emphasized the potential of early TIPS in patients with variceal bleeding.[50] TIPS is contraindicated in patients with severe hepatic failure, chronic heart failure, hepatic encephalopathy, bile duct obstruction, or cholangitis. TIPS is

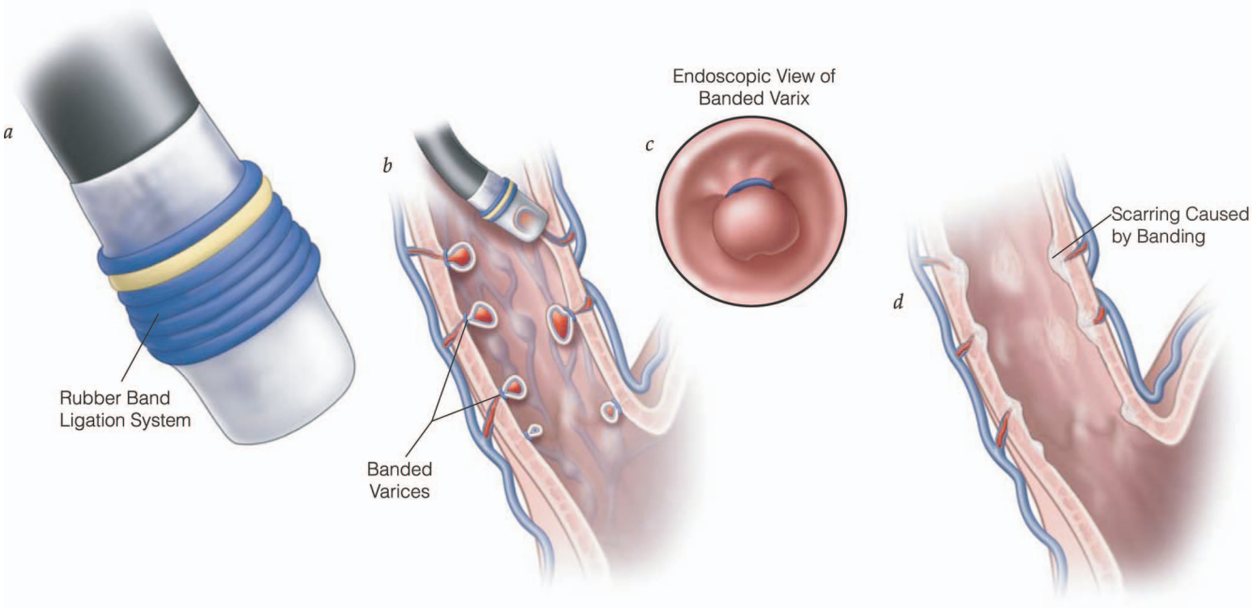

Figure 12 **Treatment of esophageal varices with banding. (*a*) The rubber band system shown in position on the endoscope is applied to varices. (*b*) The varix is suctioned into the cap of the banding system, and the band is deployed. (*c*) Shows an example of an endoscopic view of a banded varix. Bands create a wound healing response, leading to scarring with ulcer formation and collapse and obliteration of the varix. (*d*) After multiple bands have been placed, varices may be obliterated. Band ligation is currently considered the standard of care approach to management of esophageal variceal bleeding.**

reported to control bleeding in at least 90% of patients, with rebleeding rates of 12 to 26% at 1 year and 16 to 44% at 2 years.[51,52] The main problems with TIPS are occlusion of the shunt (up to 80% in 1 year) and hepatic encephalopathy (20%). Reappearance of varices on surveillance upper endoscopy or bleeding varices should prompt evaluation of the shunt by transabdominal ultrasonography. Other complications include hepatic encephalopathy, portal vein thrombosis, renal failure, sepsis, and stent migration or stenosis. The procedure-related mortality can be as high as 1 to 2%, largely from intraperitoneal hemorrhage.

Surgical intervention is rarely used for variceal bleeding; it is considered when other measures have proved ineffective. Surgical treatments include portosystemic venous shunt operations and esophageal devascularization. A variety of surgical shunts are available. These are generally classified as total, partial, or selective depending on the intended impact of portal flow diversion. The end-to-side portacaval shunt is a total shunt that diverts all portal blood flow into the inferior vena cava. The side-to-side portacaval shunt diverts only part of the portal blood flow. Selective shunts decompress variceal flow while preserving portal

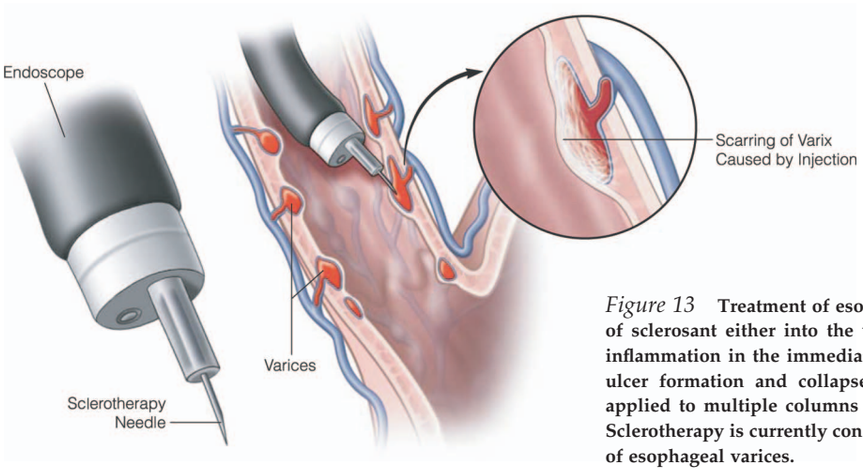

Figure 13 **Treatment of esophageal varices with sclerotherapy. Injection of sclerosant either into the varix or beside the varix creates injury and inflammation in the immediate area of the varix, leading to scarring with ulcer formation and collapse and obliteration of the varix (and when applied to multiple columns of varices, obliteration of multiple varices). Sclerotherapy is currently considered second-line therapy for the treatment of esophageal varices.**

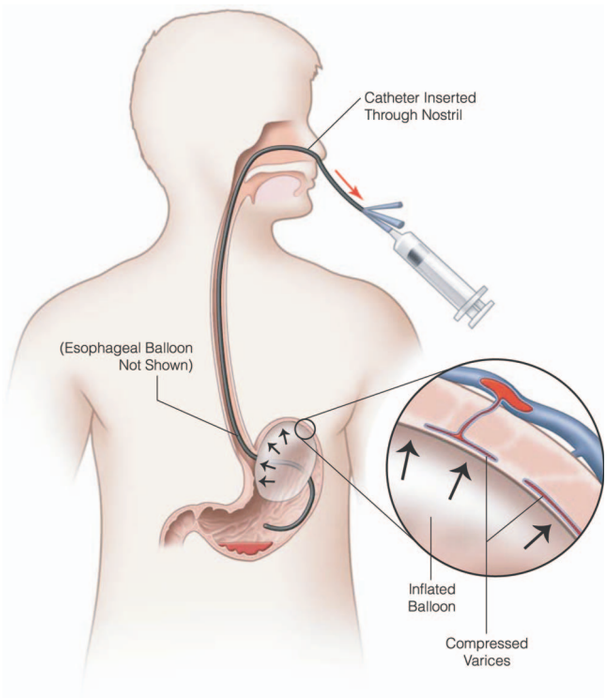

Figure 14 **Treatment of esophageal varices with balloon tamponade. The balloon-containing tube is placed into the stomach, and the gastric balloon is inflated. The gastric balloon is then pulled so that it is snug against the gastroesophageal junction. This pressure tamponades the flow of blood.**

blood flow. The distal splenorenal shunt is a selective shunt designed to prevent encephalopathy, which is often seen with total shunts. Surgical shunts can decrease rebleeding rates for both esophageal and gastric varices but do not improve survival. They may also result in encephalopathy and make future liver transplantation technically more difficult. Esophageal devascularization may be an effective means of controlling acute variceal bleeding, but bleeding can recur as additional varices develop.

MALLORY-WEISS TEAR

MW tears account for 5 to 11% of all major upper GI hemorrhages.[53] An MW tear is a longitudinal mucosal laceration at the gastroesophageal junction or gastric cardia caused by forceful retching or vomiting. During vomiting, the intra-abdominal pressure is increased with concomitant negative intrathoracic pressure, which causes a shearing effect on the mucosa. It is frequently seen in patients with hiatus hernia and vomiting associated with alcohol. Most patients present with hematemesis and generally give a history of nonbloody vomiting preceding hematemesis, although some patients do not recall vomiting. MW tears can also occur with upper GI endoscopy when a patient struggles or retches during the procedure.

Endoscopically, MW tears are noted within 2 cm of the gastroesophageal junction on the lesser curvature region of the cardia. They may or may not have stigmata of recent bleeding [*see Figure 15*]. They are usually single, although multiple tears have been reported. The tears have a low risk of recurrent bleeding and do not have to be endoscopically treated unless active oozing or bleeding is seen. An actively bleeding MW tear is best treated with endoscopic hemoclips, with the second choice being electrocoagulation.

Patients with an MW tear may be given antiemetics if they have nausea or vomiting to prevent aggravation of the tear. PPIs are often prescribed to accelerate healing, with the thought that raising gastric pH improves coagulation. However, MW tears start healing within hours and can heal completely within 48 hours. Therefore, long-term PPI therapy is not needed. Rapid healing of MW tears is also the reason that delayed endoscopy often does not show a lesion, and diagnosis of an MW tear may therefore remain a clinical diagnosis.

DIEULAFOY LESIONS

Dieulafoy lesions were defined by George Dieulafoy in 1886.[54,55] Normally, an artery is seen in the submucosa, which divides into smaller branches in the mucosa. In Dieulafoy lesions, an abnormally large, tortuous submucosal artery projects into the mucosa and can cause massive bleeding on erosion of the overlying mucosa and the arterial wall. The cause is not known. It represents up to 5% of all the causes of GIB and is commonly found in the proximal stomach, within 6 cm of the gastroesophageal junction. However, it can be found throughout the GI tract. In a review of 90 Dieulafoy lesions, 34% of the lesions were extragastric.[56] They are usually single, although more than one bleeding point from the same aberrant vessel can occur. They can be extremely difficult to detect endoscopically due to the intermittent nature of bleeding, and the overlying mucosa appears normal. Dieulafoy lesion, if found, is treated with injection therapy, a clip, a heater probe, or band ligation [*see Figure 16*]. Satisfactory hemostasis can be achieved in up to 90% patients, with 4 to 16% of cases requiring surgery.[57]

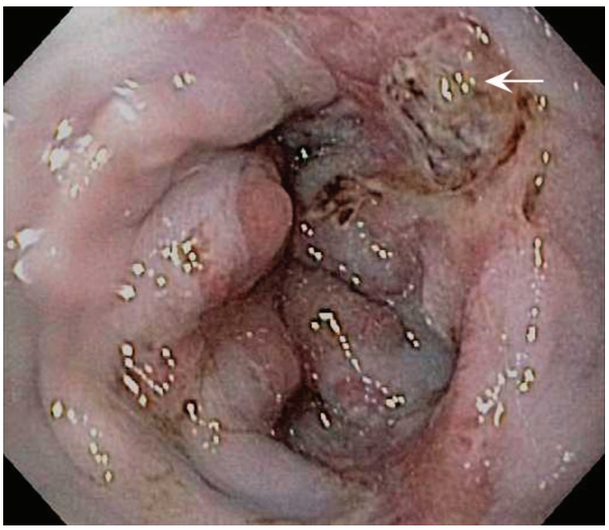

Figure 15 **Mallory-Weiss tear. A raised protuberant lesion is visible in the right upper portion of the figure (*arrow*). This was treated with epinephrine injection, with no further bleeding.**

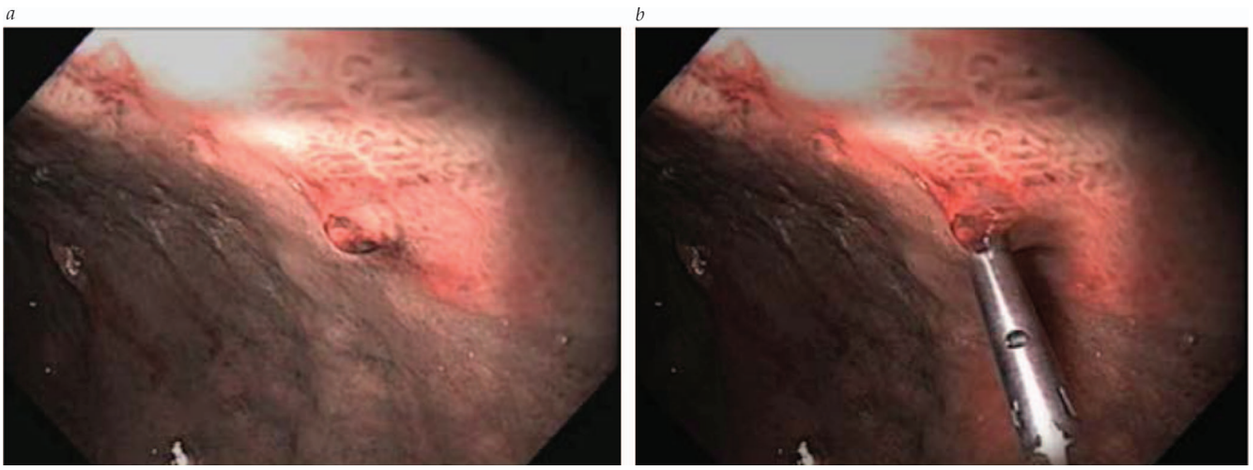

Figure 16 **Dieulafoy lesion in the rectum treated with a hemoclip. (*a*) The bleeding lesion appears as a punctum. (*b*) A single clip was placed on it, and there was no further bleeding.**

CAMERON LESIONS

Cameron lesions are linear erosions or ulcers that occur within a hiatal hernia near the diaphragmatic impression.[58] They are thought to be caused by mechanical trauma and local ischemia as the hernia moves against the diaphragm. They can cause acute GIB, although slow GIB and resultant anemia are more common. Endoscopic treatment is usually not needed. Treatment is usually with a PPI and oral iron. Surgical repair of the hiatal hernia may be needed in some cases.

GASTRIC ANTRAL VASCULAR ECTASIA

Gastric antral vascular ectasia (GAVE), also known as watermelon stomach, is classically observed endoscopically as erythematous linear streaks arising from the pylorus extending proximally into the antrum. When associated with cirrhosis, the erythema is more diffuse and can be confused with gastritis or portal gastropathy. Pathologically, GAVE is defined as ectatic mucosal blood vessels and is thought to be a response to mucosal trauma from contraction waves in the antrum. GAVE more commonly causes iron deficiency anemia and melena rather than acute bleeding. It is more common in older women and in patients with cirrhosis, scleroderma, and end-stage renal disease. Endoscopic hemostasis with thermal heat modalities such as argon plasma coagulation (APC), multipolar electrocautery (MPEC), cryotherapy, or radiofrequency ablation (RFA) is the treatment of choice. APC (noncontact method) is sometimes preferred because it is easier to treat large areas with this method. Several sessions (4 to 8 weeks apart) may be required to successfully treat all the lesions. Rarely, in severe cases not responding to endoscopic treatment, surgical antrectomy may be required.

PORTAL HYPERTENSIVE GASTROPATHY

Portal hypertensive gastropathy (PHG) is caused by increased portal pressure and increased mucosal blood flow, which results in ectatic blood vessels. It mainly involves the fundus and proximal gastric body. Endoscopically, mild PHG appears as a fine, white reticular pattern separating areas of pinkish, edematous mucosa and giving a "snake skin" appearance and is not associated with bleeding. Severe PHG appears additionally as focal or confluent cherry-red spots, which represent diffuse subepithelial hemorrhaging [*see Figure 17*]. Although this usually causes slow, chronic blood loss, acute bleeding has been reported. Treatment of PHG involves decreasing portal pressure by nonselective beta blockers (such as propranolol or nadolol), TIPS, or surgical shunts. Unlike GAVE, endoscopic treatment has no role in PHG unless a focal bleeding lesion is found. Hence, it is important to make the distinction between GAVE and PHG. This is generally not a problem

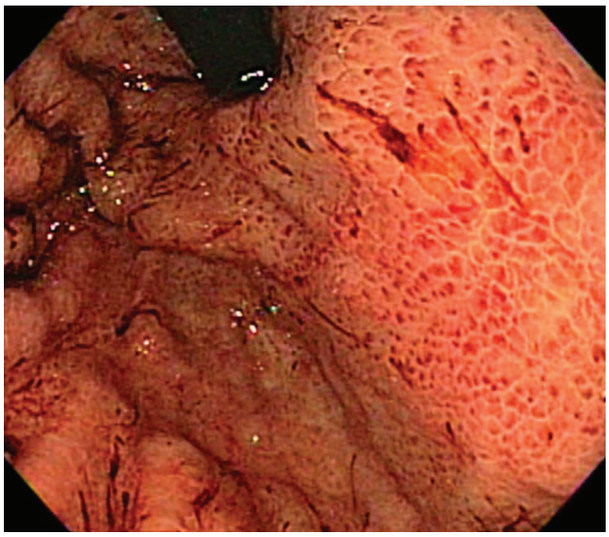

Figure 17 **Severe portal hypertensive gastropathy. The image shows a retroflexed view of the stomach, which is notable for a "snake skin" appearance, with multiple punctate, erythematous lesions with associated bleeding.**

due to location (GAVE, distal stomach; PHG, proximal stomach) and appearance (GAVE, red streaks; PHG, snake skin), but GAVE is more common in cirrhosis, and severe cases of both can resemble each other [*see Table 5*].

Lower Gastrointestinal Bleeding

LGIB is bleeding from the colon, rectum, or anal canal. LGIB that requires hospitalization represents fewer than 1% of all hospital admissions in the United States. The estimated annual incidence of LGIB is about 20 patients per 100,000, with an increased risk in older adults.[59] LGIB is somewhat more common in men than in women because the two common causes, diverticulosis and angiodysplasia, are more common in men. Initial management includes stabilization of hemodynamics, as highlighted above. The most critical decision surrounds the timing of endoscopy. An upper GI tract lesion should be considered in patients with evidence of active bleeding [*see Figure 18*], and these patients may be considered ideal candidates for urgent endoscopy (often after aggressive preparation). Patients with less aggressive bleeding can undergo expectant endoscopy, usually after a standard bowel preparation.

Diverticulosis accounts for around 30 to 50% of the cases of hemodynamically significant LGIB, whereas angiodysplasia accounts for about 20 to 30% of cases. Hemorrhoids are the most common cause of LGIB in patients younger than 50 years, but the bleeding is usually minor, and they rarely cause significant LGIB.[60,61]

DIVERTICULOSIS

Colonic diverticula are one of the most common causes of LGIB, particularly in the elderly. Colonic diverticula are herniations of colonic mucosa and submucosa through the muscular layers of the colon. These herniations usually occur at the site where blood vessels penetrate the muscular layer. Diverticulosis is much more common in Western countries (50% in older adults) compared with African or Asian countries (< 1%). This has been attributed to a low-fiber diet in Western countries, which causes constipation and hence increased intraluminal pressure.[62,63] The frequency increases with advancing age (5% at age 40, 65% at age 80), likely due to a weakening colonic wall and a decrease in muscle tone. Bleeding occurs from an arteriole at either the dome or the neck of a diverticulum. Typically, there is no associated diverticulitis.

Table 5 Differentiation of Portal Hypertensive Gastropathy and Gastric Antral Vascular Ectasia

Factors	*Portal Hypertensive Gastropathy*	*GAVE*
Location	Proximal stomach	Antrum
Endoscopic appearance	Mosaic pattern (mild) + cherry-red spots (severe)	Erythematous streaks
Treatment	Beta blockers TIPS	Endoscopic Iron supplementation

GAVE = gastric antral vascular ectasia; TIPS = transjugular intrahepatic portosystemic shunt.

It is estimated that 3 to 5% of patients with diverticulosis will bleed at some time in their lives.[64,65] The true incidence of diverticular bleeding is difficult to ascertain given the different definitions and evaluations used in various studies, and the diagnosis is often presumptive because most diverticular bleeding tends to stop spontaneously. The mean age period for diverticular hemorrhage is the sixth decade of life. The bleeding is usually abrupt, painless, and with large volume; 33% of diverticular bleeding may require emergent transfusion. Yet bleeding stops spontaneously in 70 to 80% of cases. NSAIDs have been shown to increase the risk of bleeding from diverticular disease, with over 50% of patients with bleeding diverticula consuming NSAIDs at the time of presentation.[66]

Colonoscopy remains the cornerstone for diagnosis and possible management of diverticular bleeding. However, there is some debate on the timing of colonoscopy. Proponents of early colonoscopy (within a few hours) believe that early colonoscopy increases the probability of finding the source of bleeding. However, this has not been consistently proven. Also, with early colonoscopy, usually there is not enough time for adequate colonoscopy preparation. With delayed colonoscopy, the bleeding may have stopped by the time of colonoscopy, and in such situations, colonoscopy is helpful to rule out other causes of LGIB. Recurrent diverticular bleeding is noted in up to 9% cases.[67] Hence, if a bleeding diverticulum is identified on colonoscopy, it is advisable to "tattoo" the site endoscopically for easier future identification as needed.

HEMORRHOIDS

Hemorrhoids may be external or internal. External hemorrhoids are those that occur outside the anal verge. They are sometimes painful and are often accompanied by swelling and irritation. Internal hemorrhoids are those that occur inside the rectum, above the dentate line. As this area lacks pain receptors, internal hemorrhoids are usually not painful, and most people are not aware of their presence. The most common symptom of internal hemorrhoids is bleeding characterized by bright red blood per rectum coating the outside of stool, observed on wiping or in the toilet bowl. Usually, bleeding is mild, intermittent, and self-limited, but transfusion has been reported. The diagnosis can be made with anoscopy, sigmoidoscopy, or colonoscopy, especially if performed while bleeding is ongoing. If a patient has had a normal colonoscopy within the last few years, then it is unlikely that there is a proximal colonic lesion, and only anoscopy or sigmoidoscopy may be needed. Treatment of hemorrhoids is usually medical, consisting of fiber supplementation, stool softeners, lubricant rectal suppositories, and warm sitz baths. For severe bleeding, therapeutic approaches include medical band ligation and surgical hemorrhoidectomy. Other modalities that have been attempted include injection sclerotherapy, cryosurgery, electrocoagulation, or infrared photocoagulation.

ANGIODYSPLASIA

Angiodysplasia, also termed angioectasia, is an acquired vascular ectasia that develops with advancing age. Typically, patients are 60 to 80 years old. Although endoscopically

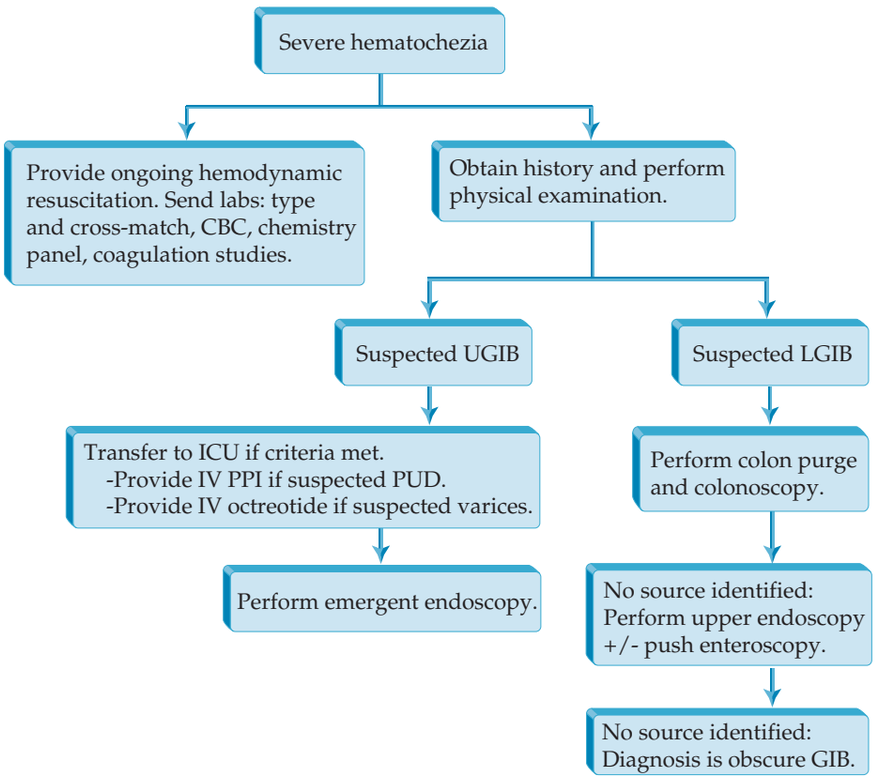

Figure 18 **Algorithm for lower gastrointestinal bleeding (LGIB). Patients with unstable hemodynamics should receive careful attention, in particular, consideration of investigation of the upper gastrointestinal tract. This is because blood is an excellent cathartic, and a large amount of blood delivered to the upper gastrointestinal tract will traverse quickly to the colon and often remain red in color. CBC = complete blood count; GIB = gastrointestinal bleeding; ICU = intensive care unit; IV = intravenous; PPI = proton pump inhibitor; PUD = peptic ulcer disease; UGIB = upper gastrointestinal bleeding.**

resembling arteriovenous malformations (AVMs), the term *AVM* is reserved for congenital lesions. The pathogenesis of angiodysplasia remains unclear, but a proposed cause is chronic, intermittent, low-grade obstruction of submucosal veins, leading to dilatation of mucosal capillaries [*see Figure 4*]. Angiodysplastic lesions are usually small (2 to 5 mm in diameter) and can be single or multiple. Large lesions appear to be more likely to bleed [*see Figure 19*]. These lesions can occur anywhere in the GI tract but are most commonly found in the proximal colon (approximately 80%), particularly the cecum.[68] Angiodysplasia is an incidental finding at colonoscopy in 2% of nonbleeding patients older than 65 years.[69,70] Fewer than 10% of angiodysplastic lesions are associated with bleeding.[69] Medical conditions associated with increased frequency of angiodysplasia include chronic kidney disease, aortic stenosis, and von Willebrand disease. In one prospective study, all patients with bleeding angioectasias compared with nonbleeding angioectasias had acquired von Willebrand disease.[71] Even aortic stenosis is associated with von Willebrand disease in 67 to 92% patients due to the disruption of von Willebrand proteins during passage of blood through the stenotic aortic valve.

Endoscopic treatment is preferred for acute bleeding. Any of the modalities—epinephrine injection, thermal probe coagulation, APC, clips, and band ligation—may be performed. About 50% of treated patients rebleed because angiodysplasia can be multifocal, and it may be difficult to identify and treat all of them, especially when located in the small bowel. However, endoscopic treatment may decrease the requirement for blood transfusions.

Medical treatment consists of oral iron and avoiding medications such as aspirin, NSAIDs, and clopidrogel. Few patients may need periodic transfusion. Hormonal therapy with estrogen and progesterone has been used with varying

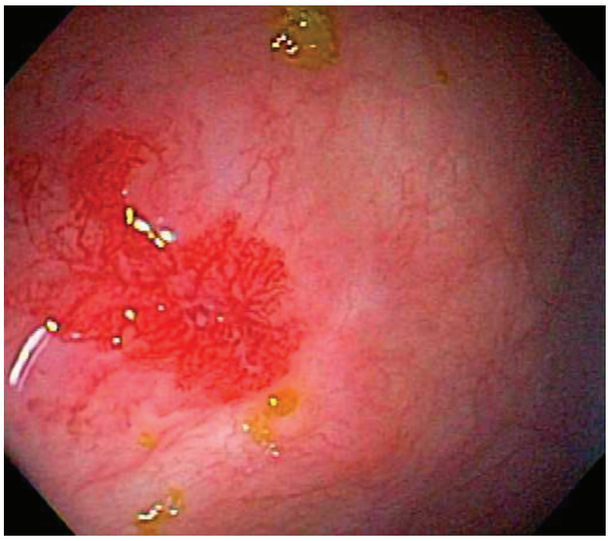

Figure 19 **Vascular ectasia. These lesions are usually small (2 to 5 mm in diameter) but can become large and can be single or multiple. These lesions can occur anywhere within the gastrointestinal tract but are most commonly found in the proximal colon, particularly the cecum.**

success for bleeding angiodysplasia.[72,73] This interest originated from the initial report of its use in a woman with Osler-Weber-Rendu syndrome whose episodes of epistaxis were dependent on her hormonal cycle.[74] The proposed mechanisms of action are reduction of bleeding times, stasis in the mesenteric microcirculation, and improvement in the integrity of the vascular endothelium.

RECTAL ULCERS

Rectal ulcers have many different causes and include the following: stercoral ulcer, stress ulcers, colitis cystica profunda, infectious ulcers, radiation-induced ulcers, NSAID ulcers, inflammatory bowel disease, malignancy, trauma, and endometriosis. Some rectal ulcers are caused by straining or abnormal defecation and are referred to as the solitary rectal ulcer syndrome (SRUS).

SRUS is a chronic, benign disorder of young adults affecting the rectum, often related to straining or abnormal defecation. SRUS is an infrequent or underdiagnosed disorder, with an estimated prevalence of one in 100,000 persons per year. The term *SRUS* probably is a misnomer because ulcers are found in only 40% of patients, whereas 20% of patients have a solitary ulcer, and the rest of the lesions vary in shape and size, from hyperemic mucosa to broad-based polypoid lesions.[75,76] The pathogenesis of SRUS is not well established but is believed to result from direct trauma or local ischemia. It is proposed that most patients have some rectal prolapse and high external anal sphincter tone. These, together with increased intra-abdominal pressure during straining, raise intrarectal pressure, which leads to venous congestion, ischemia, and ulceration. Patients usually present with passage of mucus and blood per rectum on defecation. The amount of blood varies from slight fresh blood to severe hemorrhage that requires blood transfusion. Up to 26% of patients can be asymptomatic. Active bleeding can be controlled endoscopically. Otherwise, the stepwise management includes teaching proper defecation technique, avoiding constipation by behavior modification supplemented by fiber and biofeedback, topical medications, and surgery.

Stercoral ulceration is thought to be secondary to inspissated or impacted feces causing pressure necrosis of the bowel wall. It usually occurs in elderly patients with a history of chronic constipation. The prevalence of stercoral ulceration is unknown. In autopsy studies, stercoral ulceration has been found in 1.3 to 5.7% of elderly patients in long-term care facilities.[77] The lesions commonly occur in the rectum and sigmoid colon along the antimesenteric margin. This pattern is thought to be caused by harder consistency of the stool, relatively poor blood supply, a narrow diameter, and high intraluminal pressure in this location. Complications of stercoral ulceration include bleeding and perforation. Endoscopically, the findings are of an irregular, geographically outlined ulcer that conforms to the contour of the impacted feces. Bleeding from stercoral ulcers has been successfully treated with endoscopic hemostasis, including endoscopic multipolar electrocoagulation and injection therapy. Surgical intervention is indicated if stercoral perforation or failure to control bleeding is encountered.

The term *stress ulcer* is used to describe ulcers in the rectum seen in extremely ill hospitalized, elderly patients. They may be solitary or multiple and located 3 to 10 cm above the dentate line. In one series, the median age of patients was 71 years and the average length of hospitalization was 7.5 days prior to the onset of bleeding.[78] The ulcers are thought to be a result of mucosal ischemia (like gastric stress ulcers). They often have stigmata of recent hemorrhage and can be treated endoscopically. The mortality is high due to medical comorbidities.

RADIATION PROCTITIS

Ionizing radiation can cause acute and chronic damage to the colon and rectum during treatment of gynecologic, prostate, bladder, or rectal tumors. Acute radiation proctitis occurs in the first few weeks after therapy in approximately 75% of patients who receive a radiation dose of 4,000 cGy or greater and is the result of direct epithelial damage. The symptoms include diarrhea, urgency, abdominal cramping, bleeding, and tenesmus. Acute radiation proctitis usually resolves without treatment after several months. Chronic radiation effects are seen 6 to 18 months after radiation but can occur after many years. The etiology is felt to be radiation-induced vascular damage that leads to mucosal ischemia, thickening, and ulcerations. Patients with chronic radiation injury of the rectum will have symptoms of proctitis, including tenesmus, mucoid rectal discharge, and bleeding per rectum; occasionally, constipation occurs and less commonly low-grade obstruction or fistulous tract into adjacent organs. Bleeding may be minimal to chronic and severe, requiring blood transfusion. Colonoscopy or sigmoidoscopy is required to locate the lesion and rule out tumor recurrence (because the symptoms are nonspecific), and endoscopic treatment is needed in selected cases. The endoscopic appearance includes telangiectasias (superficial dilated terminal aspect of vessel), friability, erosions, or ulcerations. Due to friability, these lesions tend to bleed easily on contact. The initial treatment focuses on avoidance of aspirin and NSAIDs, avoiding constipation with a high-fiber diet, and iron supplementation if the patient is anemic. Aminosalicylic acid derivatives (mesalamine) and corticosteroids given orally or as an enema have been used but are generally not effective.[79] Sucralfate enemas have been tried with good initial results for refractory cases, but follow-up studies are limited. Hyperbaric oxygen and antioxidant vitamins such as vitamins E and C have also been shown to reduce bleeding in chronic radiation proctitis.[80] Endoscopic methods for hemostasis mainly include thermal therapies of MPEC and APC. Recently, RFA has been successfully used to control bleeding in chronic radiation proctitis.[79] Repeated treatments are often necessary. Topical application of 4% formalin under endoscopic visualization has been shown to reduce bleeding.[81] In the United States, it is generally used as second-line therapy after the above treatments have failed. Surgery may be needed for persistent symptoms or local complications, including pelvic fistulas (e.g., vaginal or bladder) and uncontrolled bleeding.

ISCHEMIC COLITIS

Ischemic colitis may be difficult to diagnose clinically and requires a high level of suspicion. Patients with cardiovascular disease, including a history of atherosclerosis, congestive heart failure, or atrial fibrillation, should be considered likely candidates. It is important to emphasize that patients

may or may not have abdominal pain associated with ischemic colitis. Bleeding is typically modest but can be serious in rare situations. The endoscopic lesion is usually one in which large "geographic" ulcers are visualized [*see Figure 20*]; these are typically nonspecific endoscopically, so the diagnosis is made based on clinical grounds. Histology may reveal signs of ischemic injury in the mucosa.

RECTAL VARICES

Ectopic varices are defined as large portosystemic venous collaterals occurring anywhere in the abdomen except in the cardioesophageal region; they account for up to 5% of all variceal bleeding. Rectal varices are a form of ectopic varices and are reported in between 10 and 40% of cirrhotic patients undergoing colonoscopy. The frequency of rectal varices increases with the degree of portal hypertension. Approximately 60% of patients with a history of bleeding esophageal varices have rectal varices. Rectal varices may develop in patients with portal hypertension as a result of portosystemic shunting between the superior hemorrhoidal veins (portal circulation) and the middle and inferior hemorrhoidal veins (systemic circulation). Endoscopically, they are best seen on retroflexion as tortuous dilated veins extending into the rectum. They are distinct from internal hemorrhoids because they are located several centimeters above the dentate line. The treatment of rectal varices is similar to that of esophageal varices: band ligation, sclerotherapy, or a portosystemic shunt.[82,83]

POSTPOLYPECTOMY BLEEDING

Colonoscopic polypectomy is generally considered a safe procedure, but hemorrhage is reported to occur in 0.3 to 6.0% of cases.[84] In a retrospective study of 83 patients who underwent a total of 274 polypectomies, bleeding occurred at a median of 5 days (0 to 17 days) after the procedure.[85] Bleeding is associated with advanced age, polyps greater than 1 cm in diameter, sessile polyps, a thick stalk, cecal polyps, and the use of aspirin, NSAIDs, other antiplatelet drugs, and anticoagulants.[86,87] The prognosis for these patients is favorable. Most cases are managed with observation or endoscopically mediated hemostasis. Before repeat colonoscopy, whenever possible, patients should receive a rapid colonic lavage with 2 to 3 L of a nonabsorbable polyethylene glycol solution administered orally or through an NG tube over 2 hours to cleanse the colon and facilitate adequate visualization.

ANAL FISSURES

Anal fissures usually cause extremely painful bowel movement but can present with mild hematochezia that is especially noticeable on wiping. Rarely, bleeding may be severe. Causes of anal fissure include constipation, Crohn disease, ischemia, and childbirth. Initial treatment is aimed at resolving the fissure rather than specific hemostasis by eliminating constipation (fiber supplements and laxatives), softening stools, and reducing anal sphincter spasm. Sitz baths provide symptomatic relief by increasing mucosal blood flow and relaxing the sphincter. Topical medications used to treat anal sphincter spasm include nitroglycerine and calcium channel blockers such as nifedipine and diltiazem. These measures are successful in 60 to 90% of patients.[88] However, patients who do not heal or develop frequent recurrences may need botulinum toxin injection or surgery to relax the anal muscles.

CANCER AND POLYPS

Colon cancer is a relatively common cause of hematochezia but is usually associated with intermittent low-volume rather than continuous aggressive bleeding. It is important to emphasize the importance of these lesions in the differential diagnosis.[89,90] Search *ACP Medicine* for more information on colon cancer.

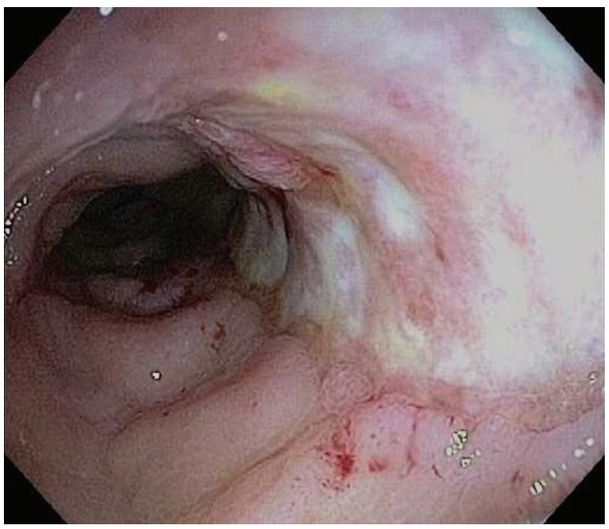

Figure 20 **Ischemic colitis. Seen is a typical large geographic ulceration with surrounding edema and abrupt transition to mucosa with an abnormal vascular pattern, often termed "dusky" in appearance.**

Obscure Gastrointestinal Bleeding

Obscure overt GIB is defined as visible GIB of uncertain etiology after nondiagnostic upper endoscopy and colonoscopy. Visible GIB may be in the form of melena, hematemesis, maroon-colored stools, or hematochezia. The reasons for not being able to localize the site include the following: (1) the bleeding site is present within the reach of the endoscope and colonoscope but not seen (hidden behind a mucosal fold; lesion already healed if done after a few days, as in a MW tear or diverticular bleeding; intermittent bleeding, as in Dieulafoy lesion) and (2) the lesion is present in the small intestine beyond the reach of the endoscope and colonoscope. Studies suggest that in 50% of cases, the bleeding site was missed or there was a difficult to visualize lesion within the endoscopic reach.[91,92] Hence, in a patient with recurrent, unexplained hematochezia or maroon-colored stools, repeat colonoscopy should be performed to evaluate for lesions that can bleed profusely and intermittently, such as diverticulosis, angiodysplasia, and Dieulafoy lesion. Similarly, if a patient has recurrent melena or hematemesis, upper endoscopy should be performed to look for missed lesions such as Dieulafoy lesions, angiodysplasia,

ulcers, and Cameron erosions. Generally, for second endoscopy, push enteroscopy is preferred instead of upper endoscopy because it allows examination of the proximal small bowel.

If repeat endoscopic procedures are negative, then evaluation should focus on the small bowel [*see Figure 21*]. The different modalities are described in an earlier section. If the bleeding is brisk, then the options are deep enteroscopy, red blood cell scanning, and angiography. It should be emphasized that with deep enteroscopy, visualization of the entire small bowel is seldom achieved, and even with a combined antegrade and retrograde approach, a segment of small bowel may not be visualized. If the bleeding is intermittent, the above tests are unfruitful; then wireless small bowel capsule diagnostic endoscopy is the preferred approach. Depending on the lesion found, an appropriate therapeutic approach is pursued.

Obscure occult GIB is usually detected when a fecal occult blood test (FOBT) is positive and there is no visible blood in stool. Normal fecal blood loss is 0.5 to 1.5 mL/day.[93] The available FOBTs can detect increased amounts of blood in stool. FOBTs can detect blood chemically or immunologically. Chemical methods (e.g., guaiac) detect the heme moiety of hemoglobin; the pseudoperoxidase activity of heme releases oxygen from hydrogen peroxide, which reacts with guaiac to form a blue dye.

Immunochemical FOBTs use monoclonal or polyclonal antibodies raised against the globin moiety of human hemoglobin, detecting intact human hemoglobin or its very early degradation products. Immunochemical tests may be of different types, including enzyme immunoassay, reverse passive hemagglutination, latex agglutination inhibition assay, and latex agglutination assay. A guaiac test depends on peroxidase activity in feces and is not specific to

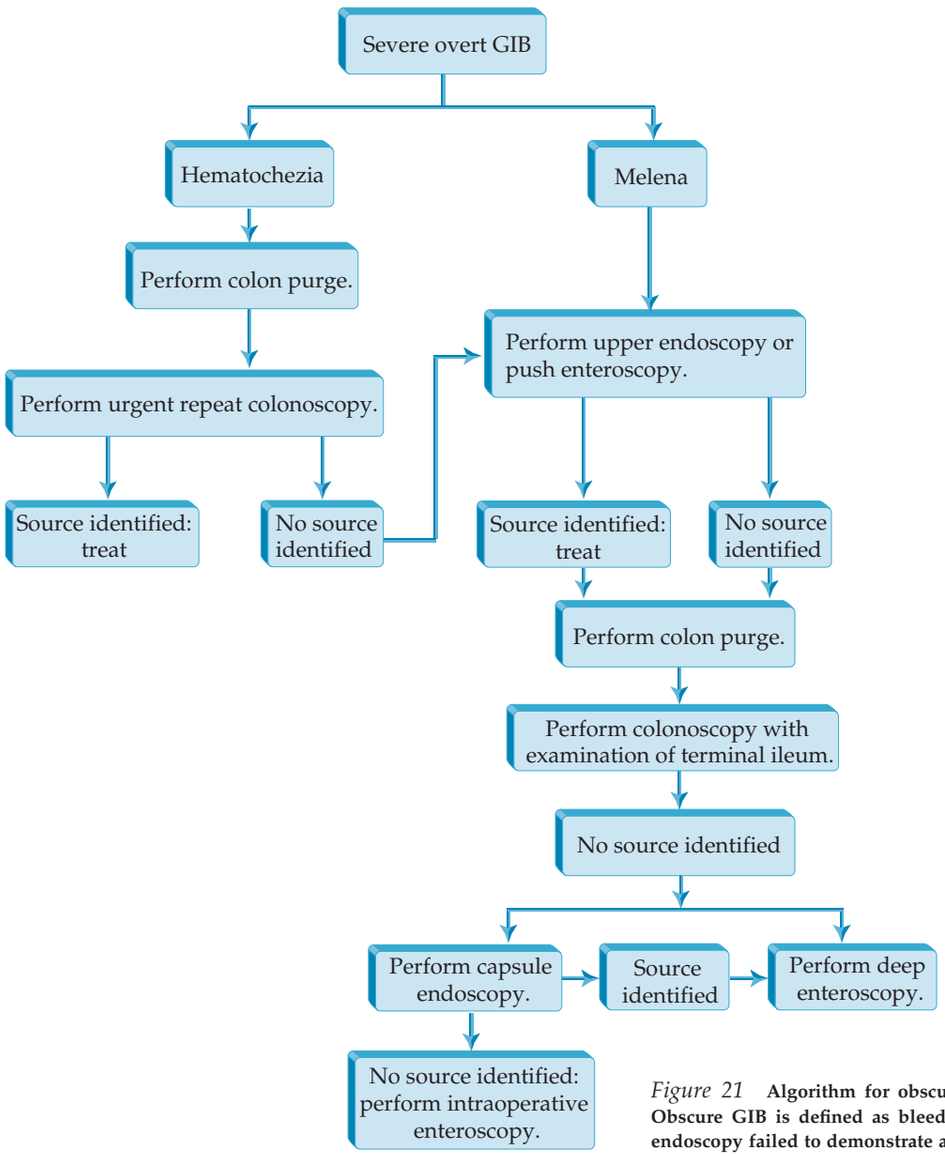

Figure 21 **Algorithm for obscure gastrointestinal bleeding (GIB). Obscure GIB is defined as bleeding after routine upper and lower endoscopy failed to demonstrate a lesion.**

peroxidase in human hemoglobin. Hence, a number of variables may influence guaiac test results that do not influence the results of immunochemical tests. These include ingestion of animal hemoglobin; myoglobin in red meat, fruit, and vegetables high in peroxidase activity; and aspirin or other medication that may produce GIB, each of which may cause false positive results. Immunochemical tests are not influenced by these extraneous factors, and patients do not have to modify their diets or medications for the test. It is important to know what type of FOBT is offered locally so that appropriate instructions can be given to the patient. Immunochemical tests are considered to have better sensitivity (at the cost of specificity), but, overall, the two tests can be considered comparable (< 50% for detection of all neoplasms and 50% for detection of colorectal cancer).[94–96]

The approach to a patient with positive FOBT depends on the reason the test was performed. If FOBT was performed for colon cancer screening, then the patient should undergo colonoscopy. When used for colon cancer screening, at least three (preferably six) stool samples should be checked before calling the result negative. Any positive FOBT is considered significant. If FOBT was performed for iron deficiency anemia, then the patient should undergo both upper endoscopy and colonoscopy. However, some argue that upper endoscopy should be performed in all cases of positive FOBT (guaiac based, irrespective of anemia or iron studies). This is based on a study of 248 patients with positive FOBT in whom more lesions were found on upper endoscopy (esophagitis, gastritis, ulcers) than on colonoscopy (adenomas and cancer).[97] If the upper endoscopy and colonoscopy are negative, then small bowel evaluation with capsule endoscopy or enteroscopy should be performed. Occult GIB causes most cases of iron deficiency in adults, especially in men and postmenopausal women, and should be considered in cases of unexplained iron deficiency anemia. Most of the lesions that cause overt bleeding can also produce occult blood loss. However, variceal and diverticular hemorrhage invariably bleed overtly, whereas lesions such as angiodysplasia, GAVE, PHG, and Cameron erosions tend to result in occult bleeding. FOBT can be checked on spontaneously passed stools or stool obtained on a digital rectal examination. A digital rectal examination can potentially give a false positive result due to trauma to the mucosa in the anal canal, but several studies have refuted this concept. Hence, a positive FOBT should be approached the same way, irrespective of how the sample was obtained.

Lesions that can cause obscure GIB are many of those that can cause typical upper or lower GI tract bleeding [*see Table 1*]. Important causes of obscure bleeding include those highlighted in Table 6. The cause of bleeding is more likely to be Meckel diverticulum, Crohn disease, or tumor in patients under 40 years of age and angioectasias or NSAID-induced ulcer in patients over 40 years. Angioectasias were described in an earlier section. A brief description of other conditions is mentioned below.

Table 6 Uncommon Causes of Obscure Gastrointestinal Bleeding

Hemobilia
Hemosuccus pancreaticus
Aortoenteric fistula
Atypical varices (any location)
Meckel diverticulum
Small bowel diverticulum
Dieulafoy ulcers (any location)

MECKEL DIVERTICULUM

A Meckel diverticulum is a true congenital diverticulum originating as a blind intestinal pouch from incomplete obliteration of the vitelline duct during gestation.[98] The characteristic features have been described by the rule of "2's": 2% of the population, 2 feet from the ileocecal valve, 2 inches in length, 2% are symptomatic, 2 types of common ectopic tissue (gastric and pancreatic), 2 years is the most common age at clinical presentation (with intestinal obstruction), and 2 times more commonly seen in males. The complications may include obstruction, bleeding, and diverticulitis, which can occur at any age. The bleeding is usually painless, occurs without warning, and stops spontaneously. Occasionally, Meckel diverticulitis may present with all the features of acute appendicitis. Ectopic gastric tissue–secreting acid is present in 50 to 75% of patients, which can cause ulcerations. A technetium-99m pertechnetate scan is the investigation of choice to diagnose Meckel diverticulum. This scan detects gastric mucosa and is displayed as a spot on the scan distant from the stomach. A Meckel diverticulum scan has almost 100% specificity but is negative in patients in whom the diverticulum does not contain gastric tissue.[99] There are recent reports of Meckel diverticulum diagnosed by capsule endoscopy and deep enteroscopy. Treatment is surgical.

SMALL INTESTINAL DIVERTICULA

Small intestinal diverticula are present in about 20% of the population, with increasing frequency as a function of age.[100–102] In one large series, 79% of them were located in the duodenum, 18% in the jejunum or ileum, and 3% in all three segments.[100] Duodenal diverticula are usually located within 1 to 2 cm of the ampulla, and bleeding is rare. When it occurs, the bleeding can usually be controlled endoscopically.[103] Bleeding from jejunal or ileal diverticula is quite rare.

SMALL INTESTINAL NEOPLASMS

Small intestinal neoplasms comprise only 5 to 7% of all GI tract neoplasms but are the most common cause of obscure occult GIB in patients under 50 years.[104] The most common small intestinal neoplasms are adenomas (usually duodenal), hamartomatous polyps (Peutz-Jeghers polyps, juvenile polyps), carcinoids (usually ileal), gastrointestinal stromal tumors (GISTs), lymphomas, hamartomatous polyps, and adenocarcinomas.

SMALL INTESTINAL DIEULAFOY LESION

Dieulafoy lesions of the small bowel are rare. They can occur anywhere in the small intestine. Patients tend to be younger when compared with patients with gastric Dieulafoy lesions. They can be quite difficult to find because they bleed intermittently. It is important to perform a study when the patient is actively bleeding. Deep enteroscopy and angiography are the preferred modalities.[105]

NSAID-INDUCED SMALL INTESTINAL EROSIONS

With the introduction of WCE, mucosal lesions of the small intestine are now easier to detect. Studies have reported erosions or ulcers in 25 to 55% of patients who take full-dose NSAIDs.[106–108] They usually cause occult bleeding and resolve with discontinuation of the drug. Overt bleeding can be treated endoscopically.

BLUE RUBBER BLEB NEVUS SYNDROME

Blue rubber bleb nevus syndrome is a syndrome characterized by multiple cutaneous venous malformations in association with visceral lesions, most commonly affecting the GI tract.[109,110] On endoscopy, lesions appear as larger, protuberant, polypoid, bluish blebs that can occur anywhere in the GI tract (more commonly in the small bowel and colon). Endoscopic band ligation is the preferred treatment, but it may not be possible to pass the band ligating device deep into the small bowel. Surgical resection is the alternative.

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Figures 1 to 6, 8, 10, and 12 to 14 Christine Kenney