The diagnosis and management of patients with obscure gastrointestinal (GI) bleeding was challenging for the gastroenterologist until the development of small bowel capsule endoscopy and double-balloon enteroscopy (DBE). Both of these techniques have revolutionized the management of patients with obscure GI bleeding. Detection of lesions such as small intestinal angioectasia has become possible with the advent of capsule endoscopy, and therapy of such lesions can be accomplished with DBE, without the need for intraoperative enteroscopy. The goal of this review is to shed light on the recent paradigm shift to the use of endoscopy in the diagnosis and management of patients with obscure GI bleeding.

Obscure GI bleeding, defined as bleeding from the GI tract that persists or recurs without an obvious etiology after esophagogastroduodenoscopy (EGD), colonoscopy, and radiologic evaluation of the small bowel such as small bowel follow-through or enteroclysis, could be categorized into obscure overt and obscure occult bleeding based on the presence or absence of clinically evident bleeding.

Occult GI bleeding is detected by fecal occult blood testing. There is no recent publication that recommends or has studied the role of fecal occult blood testing beyond the clinical context of colorectal cancer screening. A fecal occult blood test should be performed only in the appropriate context of colorectal cancer screening. If the test result is positive and the findings of a recommended colon cancer screening workup are negative, in the absence of iron deficiency anemia and GI symptoms, no further workup is recommended. If associated (iron deficiency) anemia is present, and if the clinical presentation satisfies the definition of obscure GI bleeding, then only it should be worked up as obscure GI bleeding.

Obscure GI bleeding could be due to lesions that are overlooked in the esophagus, stomach, and colon during initial workup or lesions in the small intestine that are difficult to visualize with conventional endoscopy and radiologic imaging. Explanations for overlooking a lesion and missing the diagnosis include lesions that have stopped bleeding during endoscopic examination, lesions that are obscured by blood clots that are unable to be mobilized during endoscopy, hypovolemia and significant anemia causing lesions to look less obvious, and intermittent and slow bleeding leading to negative findings on endoscopic and nuclear scans.

Overall, lesions in the small intestine account for approximately 5% of causes of obscure GI bleeding. Medical imaging of the small intestine has been a very difficult and limited undertaking. Several factors account for the difficulty encountered in small bowel visualization. The length of the small intestine, in addition to its free intraperitoneal location, vigorous contractility, and overlying loops, confounds the usual diagnostic techniques. These attributes limit the diagnostic ability of barium studies, endoscopic intubation, and the identification of specific sites by the special imaging techniques of nuclear medicine scans and angiography. In patients with obscure GI bleeding, the bleeding rate may be slow or intermittent, thereby not allowing identification by either angiography or bleeding scan. The yield of a small bowel series for diagnosing tumors of the small intestine is quite low and barium studies, even enteroclysis, cannot diagnose angiectasias, which are the most common causes of small intestinal bleeding. The distal small intestine has been relatively inaccessible to endoscopic intubation despite the development of various endoscopes. Because of the inability to localize a bleeding site in the small bowel, patients with obscure GI bleeding typically present with prolonged occult blood loss or recurrent episodes of melena or maroon stool without a specific diagnosis. In this group of patients, an early diagnosis of the bleeding site has been the exception rather than the norm until recently with the development of capsule endoscopy and DBE.

A MEDLINE search of English-language publications was performed from 1966 to June 2006 related to obscure GI bleeding by using the following search terms: obscure GI bleeding, occult GI bleeding, video capsule endoscopy,
and enteroscopy. Reference lists from relevant manuscripts were also inspected to identify additional applicable articles missed with the above search strategy. The following sections describe recent advances in our understanding of the etiology, diagnosis, and management of obscure GI bleeding since the publication of American Gastroenterological Association medical position statement entitled “Evaluation and Management of Occult and Obscure Gastrointestinal Bleeding” in 2000. Studies published only as abstracts were excluded. For assessment of procedural outcomes, case series were not included. To calculate yearly probabilities, the formula $p = 1 - e^{(-rt)}$ was used, where $p$ represents probability, $r$ represents rate, and $t$ represents time.

**Etiology**

Causes of obscure GI bleeding may potentially include any lesion from the oral cavity to the anorectum that may bleed into the GI tract (see Table 1). To date, there are no longitudinal or population-based studies on the frequency and location of specific causes of obscure GI bleeding.

Commonly overlooked lesions in the upper GI tract include Cameron’s erosions in large hiatal hernias,6 fundic varices,7,8 peptic ulcer disease, angioectasias,6 Dieulafoy’s lesion,9 and gastric antral vascular ectasia.10,11 Lesions missed during colonoscopy include angioectasias and neoplasms.12

The etiology of small intestinal bleeding is dependent on the age of the patient. Patients younger than 40 years are more likely to have small intestinal tumors (such as lymphomas, carcinoid tumors, and adenocarcinoma, and polyps from hereditary polyposis syndrome), Meckel’s diverticulum, Dieulafoy’s lesion, and Crohn’s disease. Patients who are older than 40 years are more prone to bleeding from vascular lesions, which comprise up to 40% of all causes, and nonsteroidal anti-inflammatory drug (NSAID)-induced small bowel disease. Less common etiologies of bleeding, which originate in the C-loop of duodenum, include hemobilia in patients with liver biopsy, trauma, and hepatocellular cancer, hemosuccus pancreaticus in patients with necrotizing pancreatitis or pancreatic transplantation, and aortoenteric fistula in patients with prior abdominal aortic aneurysm repair.

Approximately 5% of patients presenting with GI hemorrhage have no source found by upper endoscopy and colonoscopy. In approximately 75% of these patients, responsible lesions can be detected in the small bowel.14–16 In patients presenting with obscure overt bleeding (defined as the presence of recurrent melena or hematochezia with normal evaluation by upper endoscopy and colonoscopy), small bowel angiectasias are detected in 30%–60% of examinations.17

Recent advances in endoscopic imaging of the small intestine provide us an opportunity to revisit the traditional definitions of the source of GI bleeding. GI bleeding has been defined as upper or lower GI bleeding based on the location of the bleeding either proximal or distal to the ligament of Treitz. Reclassifying GI bleeding (and obscure GI bleeding) into 3 categories (upper, mid, and lower GI bleeding) instead of adhering to the traditional classification of upper GI and lower GI bleeding may be useful to improve our understanding of the problem. Bleeding above the ampulla of Vater, within the reach of an EGD, is defined as upper GI bleeding; small intestinal bleeding from the ampulla of Vater to the terminal ileum, best investigated by capsule endoscopy and DBE, is defined as mid GI bleeding; and colonic bleeding is defined as lower GI bleeding, which can be evaluated by colonoscopy.18

Angiectasias are ectatic blood vessels made of thin wall with or without endothelial lining. Small arteriovenous communications are often present due to incompetence of the precapillary sphincter. Although they are often incidentally identified during endoscopic procedures, they are increasingly recognized as a major cause of GI bleeding, particularly in the elderly. The factors that trigger these common incidentally detected lesions to present with obscure and often clinically overt GI bleeding have not been clearly elucidated.

The association of abnormal von Willebrand’s factor (vWF) is receiving increasing attention in the management of patients with bleeding GI angiectasias. Von Willebrand’s disease is a bleeding disorder that results from a qualitative or quantitative defect in vWF. vWF is a complex multimeric glycoprotein present in platelets, plasma, and subendothelium. vWF is essential to platelet adhesion and aggregation at the site of vascular injury. In an elegant study of patients with both bleeding and nonbleeding angiectasias of the GI tract and control patients with colonic diverticular hemorrhage, Veyradier et al showed that most patients with bleeding angiectasias of the GI tract lack the largest multimers of vWF.

<table>
<thead>
<tr>
<th>Table 1. Etiology of Obscure GI Bleeding</th>
</tr>
</thead>
<tbody>
<tr>
<td>Upper GI and lower GI bleeding</td>
</tr>
<tr>
<td>overlooked</td>
</tr>
<tr>
<td>Upper GI lesions</td>
</tr>
<tr>
<td>Cameron’s erosions</td>
</tr>
<tr>
<td>Fundic varices</td>
</tr>
<tr>
<td>Peptic ulcer</td>
</tr>
<tr>
<td>Angiectasia</td>
</tr>
<tr>
<td>Dieulafoy’s lesion</td>
</tr>
<tr>
<td>Gastric antral vascular ectasia</td>
</tr>
<tr>
<td>Lower GI lesions</td>
</tr>
<tr>
<td>Angiectasia</td>
</tr>
<tr>
<td>Neoplasms</td>
</tr>
<tr>
<td>Mid GI bleeding</td>
</tr>
<tr>
<td>Younger than 40 years of age</td>
</tr>
<tr>
<td>Tumors</td>
</tr>
<tr>
<td>Meckel’s diverticulum</td>
</tr>
<tr>
<td>Dieulafoy’s lesion</td>
</tr>
<tr>
<td>Crohn’s disease</td>
</tr>
<tr>
<td>Celiac disease</td>
</tr>
<tr>
<td>Older than 40 years of age</td>
</tr>
<tr>
<td>Angiectasia</td>
</tr>
<tr>
<td>NSAID enteropathy</td>
</tr>
<tr>
<td>Celiac disease</td>
</tr>
<tr>
<td>Uncommon</td>
</tr>
<tr>
<td>Hemobilia</td>
</tr>
<tr>
<td>Hemosuccus pancreaticus</td>
</tr>
<tr>
<td>Aortoenteric fistula</td>
</tr>
</tbody>
</table>
induced by a latent acquired form of von Willebrand’s disease. Because these specific multimers are the most effective in inducing platelet aggregation in condition of high shear stress that is commonly present in the microcirculation of angioectatic lesions, it was concluded their deficiency contributes to active bleeding.

Bleeding from angiectasias in patients with aortic stenosis, called Heyde’s syndrome, has been recently reviewed. Whether such an association actually exists has been questioned by an earlier prospective study, while a more recent larger but retrospective study lent support in its favor. In patients with aortic stenosis, the aortic wall shear stress is high. At such high macrovascular shear stress, increased consumption of high-molecular-weight multimers of vWF appears to occur possibly related to the increased activity of the shear-dependent vWF-cleaving metalloprotease. This leads to a relative deficiency of high-molecular-weight multimers of vWF, leading to clinically manifest bleeding from angiodysplastic lesions in the GI tract. Support for this hypothesis comes from the fact that after aortic valve replacement, the severity of bleeding from these lesions decreases along with an increase in the level of the circulating high-molecular-weight multimers of vWF. Presumably other factors such as tissue hypoxemia due to reduced GI mucosal perfusion related to hemodynamically significant aortic stenosis might play a role in this situation. Thus, this may be an urban legend; even if there is an association, it is weak and often exaggerated.

It is possible that similar pathophysiology can occur in the setting of other common cardiovascular disorders such as severe peripheral vascular occlusive disease and may help explain why elderly people often develop recurrent GI bleeding or iron deficiency anemia from bleeding angiectasias in the GI tract.

The issue of specific coagulation disorders in patients with bleeding GI angiectasias was also recently studied in a prospective cohort of 21 patients. Plasma levels of vWF, D-dimer, and tissue plasminogen activator activity were significantly different in patients with GI angiectasia compared with control patients with bleeding duodenal ulcer. The plasminogen activator inhibitor type 1 was shown to be an independent predictor of future bleeding in these patients on multivariate analysis.

Angiectasias are usually distinguished from telangiectasias, which, although anatomically similar, are usually referred to in the context of systemic or hereditary diseases. Hereditary hemorrhagic telangiectasia (HHT, Rendu–Osler–Weber syndrome) is one of the most well-known hereditary entities associated with obscure GI bleeding. Most patients with HHT will have a history of epistaxis that tends to antedate development of cutaneous or visceral telangiectasias by a decade or more. In a recent report from Denmark, the overall incidence of GI bleeding was 33% in patients with HHT and appeared to develop in the fourth or fifth decade of life. HHT is an autosomal dominant disease with high penetrance, and prevalence is estimated to range from 1:40,000 to 1:100,000. The gene for HHT has been located on chromosome 9q3, and there are 2 disease types described as HHT1 and HHT2, caused by mutations in the endoglin and ALK1 genes, respectively. HHT1 has been associated with a higher frequency of visceral manifestations, including GI bleeding, and HHT2 is believed to be associated with a lower penetrance and milder disease manifestations.

Blue rubber bleb nevus syndrome is a rare disorder characterized by the development of cavernous hemangiomas, which most commonly involve the skin and the GI tract. The most common presentations of blue rubber bleb nevus syndrome are either the appearance of the skin lesions alone or iron deficiency anemia. Most patients with GI bleeding are asymptomatic and generally respond to a blood transfusion and an iron supplement given orally. The lesions can also cause numerous extraintestinal problems such as orthopedic deformities, central nervous system involvement, spinal cord compression, disseminated intravascular coagulation, thrombocytopenia, hemothorax, and hemopericardium. Blue rubber bleb nevus syndrome is a rare, probably inherited disorder that frequently presents as GI blood loss for which endoscopic therapy and surgery is often of value.

**Evaluation**

**History and Physical Examination**

The importance of a thorough history and physical examination cannot be overemphasized in the evaluation of a patient with obscure GI bleeding. The nature of the exact presenting symptom is important in deciding a practical, efficient, and cost-effective evaluation plan. For example, recurrent hematemesis from an unknown source usually signifies a bleeding lesion above the ligament of Treitz, and lower GI evaluations are generally not warranted in such a scenario. Severity and temporal pattern of the associated anemia should have a significant impact on subsequent management decisions. For example, in a patient with mild anemia and a very slow decrease in hematocrit who has multiple severe comorbidities, a conservative workup may be prudent, although little information is available on the safety and efficacy of such a strategy. Also, the degree of severity of anemia has a bearing on planning endoscopic evaluation in terms of potential complications related to sedation.

Although abdominal symptoms may sometimes help in targeting focused evaluation, conclusions from few available studies are too divergent to recommend targeted evaluation based on abdominal symptoms. A thorough history of consumption of prescription and over-the-counter medications is very important to exclude...
Institute transfusion and may be missed in an anemic patient. In tum. The lesions are often more prominent after blood more legs radiating from an eccentrically placed punctum. The lesions develop primarily on the lips, nasal mucosa, elevated lesions with an ill-defined border and one or tympanic membrane. They appear as dark red, slightly under the nails, on the soles of the feet, and even on the tongue, palms, and palate, but they also can be found lesions with an ill-defined border and one or more legs radiating from an eccentrically placed punctum. The lesions are often more prominent after blood transfusion and may be missed in an anemic patient. In patients with blue rubber bleb nevus syndrome, classically the skin lesions present in childhood but can develop later in life. They are usually blue in color and easily compressible with light palpation. Complete compression classically results in an empty, slowly refilling sac.

Other rare causes of obscure GI bleeding with cutaneous lesions, vascular ectasias, account for up to half of the cases. Repeat EGD should be considered in patients with hematemesis and in those taking NSAIDs and the fundus should be carefully examined, with special attention to the site of diaphragmatic hiatus for Cameron’s lesion, which remains an underrecognized etiology of obscure GI bleeding. In addition, a transparent cap (band-ligator cap after deploying the bands) fitted to the end of the endoscope may serve as a retractor to examine the blind areas of the upper GI tract, such as the posterior and inferior wall of the duodenum, antrum, high lesser curve, and anastomotic sites, for ulcers and is helpful in uncovering hidden ulcers. If a capsule endoscopy is performed, instead of repeating the EGD, careful review of the capsule endoscopic images of the stomach and colon might be useful in the detection of lesions missed on prior EGD, such as gastric antral vascular ectasias and inflamed pyloric canal polyp, although the capsule is unlikely to reveal sources of bleeding that are only seen on retroflexed view of the stomach.

Although the yield of repeat colonoscopy is low (6%), it may be useful in the diagnosis of cancers that were overlooked during initial endoscopy, especially in elderly patients. Use of naloxone may improve the detection of colonic angiectasias that were not obvious at index examination. Close review of the capsule endoscopic examination of the proximal colon may identify right-sided colon cancer and cecal angiectasias.

In patients with a history of abdominal aortic aneurysm repair, the possibility of an aortoenteric fistula should be seriously considered, and examination of the c-loop of the duodenum, especially the third portion of the duodenum, should be undertaken with a pediatric colonoscope or an enteroscope. Endoscopic findings in these patients may include blood clots in the second part of the duodenum, an ulcer with black spots in the descending duodenum distal of the papilla of Vater, and submucosal hemorrhages in the stomach, or they may even be normal. Clear documentation of a fistula may not be possible, and the delay in diagnosis and surgery could be life-threatening.

Endoscopy with duodenal biopsies is the mainstay for diagnosing celiac disease. Although characteristic endoscopic features may be useful, their absence does not exclude celiac disease. Random biopsy, even of normal-appearing mucosa, is necessary for the diagnosis of celiac disease. Magnification endoscopy with chromoendoscopy is a promising technique for the evaluation of patients with suspected malabsorption. This technique is especially valuable in patients with partial atrophy, where villous abnormalities can be patchy and the duodenum usually appears normal during standard endoscopy. The yield of random small bowel biopsies in patients

**Repeat standard endoscopy.** Lesions overlooked during prior EGD, such as Cameron’s lesions, Dieulafoy’s lesions, vascular ectasias, peptic ulcers, and gastric antral vascular ectasias, account for up to half of the cases. Repeat EGD should be considered in patients with hematemesis and in those taking NSAIDs and the fundus should be carefully examined, with special attention to the site of diaphragmatic hiatus for Cameron’s lesion, which remains an underrecognized etiology of obscure GI bleeding. In addition, a transparent cap (band-ligator cap after deploying the bands) fitted to the end of the endoscope may serve as a retractor to examine the blind areas of the upper GI tract, such as the posterior and inferior wall of the duodenum, antrum, high lesser curve, and anastomotic sites, for ulcers and is helpful in uncovering hidden ulcers. If a capsule endoscopy is performed, instead of repeating the EGD, careful review of the capsule endoscopic images of the stomach and colon might be useful in the detection of lesions missed on prior EGD, such as gastric antral vascular ectasias and inflamed pyloric canal polyp, although the capsule is unlikely to reveal sources of bleeding that are only seen on retroflexed view of the stomach.

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with occult GI bleeding and iron deficiency anemia for celiac disease may be as high as 12%.48,49

It is recommended that gastroenterologists use a side-viewing endoscope to examine the ampulla in patients with hemobilia and hemosuccus pancreaticus.

**Small bowel series and enteroclysis.** The role of small bowel series and enteroclysis in the evaluation of obscure GI bleeding has declined substantially with the advent of capsule endoscopy because of its extremely low diagnostic yield. Compared with small bowel radiography, the diagnostic yield of capsule endoscopy is higher in the detection of small bowel lesions (67% vs 8%; \( P < .00001 \)) and clinically significant findings (42% vs 6%) with a number needed to treat of 3.50,51 Neither of these radiographic studies can diagnose angiectasias, which are the most common cause of small intestinal bleeding.4,5,52

In a recent retrospective review of enteroclysis in 98 patients, it was believed to change management in only 10% of patients.53 In a study of 20 patients with obscure GI bleeding, no patient with negative findings on capsule endoscopy had positive findings on enteroscopy and small bowel follow-through.54 Unless the clinical findings suggest small bowel obstruction due to malignancy, Crohn’s disease, or prior use of NSAIDs, there is no role for either small bowel series or enteroclysis in the evaluation of obscure GI bleeding.

**Cross-sectional imaging.** Novel cross-sectional imaging techniques for evaluation of small bowel include helical CT enteroclysis, helical CT angiography, and magnetic resonance enteroclysis.

Helical CT enteroclysis combines standard enteroclysis to distend the small bowel followed by helical CT.55 CT enteroclysis is superior to magnetic resonance enteroclysis in the detection of small bowel pathology.56 Few recent reports suggest the utility of helical CT in identifying small and large intestinal bleeding angiectasias.57,58

CT angiography involves catheterization of the abdominal aorta followed by helical CT angiography before and after intra-arterial injections of a contrast medium, and the site of hemorrhage is recognized as a hyperdense area due to the extravasation of contrast medium in the intestinal lumen. In a prospective study of 18 patients with bleeding colonic angiectasias, the sensitivity, specificity, and positive predictive value of helical CT angiography were 70%, 100%, and 100%, respectively, when compared with a gold standard of colonoscopy and mesenteric angiography.59 In a report of 22 patients with obscure GI bleeding, CT enteroclysis was found to be inferior to capsule endoscopy in the detection of potential bleeding lesions such as angiectasias in the small bowel.60

**Nuclear scans.** The role of nuclear scans and, in particular, technetium-99m-labeled red blood cell scans continues to be limited in patients with obscure GI bleeding. The nuclear scans may be positive in a significant proportion of patients presenting with rapid bleeding, particularly in delayed images obtained 3–4 hours after injection of the radioactive material. The ability to localize the source of bleeding, especially in the foregut, has been repeatedly demonstrated to be poor.61

**Angiography.** The data on the clinical utility of angiography in the specific setting of obscure GI bleeding are very limited. Arguably, angiography may detect both acutely bleeding and nonbleeding lesions (particularly angiectasias, which often have characteristic angiographic features) and also offers a therapeutic option with embolization if a bleeding lesion is identified. There have been a few recent reports of provocative angiography.62–64 A small case series suggests that although provocative angiography can be performed safely, the overall yield of this technique is low.62

**Endoscopic imaging.** Until recently, most of the small intestine has been relatively inaccessible to endoscopic imaging and therapy without surgery. Because of the inability to localize a bleeding site in the small bowel, early diagnosis of the bleeding site was rarely made in patients with obscure GI bleeding. Complete endoscopic imaging of the small intestine has certainly evolved from an invasive intraoperative endoscopy to a noninvasive examination of the entire small intestine with capsule endoscopy. Recently, the development of DBE has allowed us to offer endoscopic hemostatic therapy without the need for laparotomy. In between these 2 periods, Sonde enteroscopy and push enteroscopy were utilized to diagnose and manage this problem. The following sections describe each endoscopic modality and the evidence that supports their use in patients with obscure GI bleeding. For assessment of procedural outcomes, case series were not included.

**Intraoperative enteroscopy.** Intraoperative enteroscopy, involving insertion of an endoscope through an incision in the mid-small intestine (enterotomy), was initially performed in the 1950s with a sterile rigid sigmoidoscope passed through an operative colotomy or enterotomy.65 By the 1970s, fiber-optic endoscopes were being used intraoperatively.66 In 1980, Bowden et al performed intraoperative enteroscopy by passing a fiber-optic colonoscope first orally and then analy while the surgeon manually telescoped the bowel over the tip of the endoscope.67 The terminal ileum can be reached in more than 90% of patients using this technique, while minimizing the mortality and morbidity associated with enterotomy for earlier intraoperative enteroscopy procedures.68 Unlike standard endoscopy, the mucosa should be examined carefully during intubation because trauma induced by insertion of the endoscope and bowel manipulation can be confused with angiectasias upon withdrawal of the enteroscope.

The diagnostic yield of intraoperative enteroscopy in patients with obscure GI bleeding has ranged between 58% and 88% (Table 2).68–76 Laparoscopy and exploratory laparotomy with intraoperative endoscopy remain im-
important diagnostic tools for evaluation of an obscure cause of GI bleeding. In a recent case series of 25 patients with obscure GI bleeding, intraoperative enteroscopy enabled complete evaluation of the small intestine in all and resulted in a therapeutic intervention in 16 patients; over a 19-month follow-up period, there was no recurrence of bleeding in the majority (70%) of these patients. Intraoperative enteroscopy is associated with significant morbidity, including ileus, and high mortality rates up to 17%. Despite intraoperative enteroscopy, bleeding has been reported to recur in 12.5%–60% of patients because pathology is overlooked due to limited visibility and/or due to the evanescent nature of ectasias. Therefore, this technique currently is reserved as a last option or if DBE cannot be successfully performed due to the presence of abdominal adhesions or other technical factors.

**Sonde enteroscopy.** Sonde enteroscopy involves peroral placement of a long (3-m) enteroscope with a distal balloon into the proximal small intestine that is propelled by peristaltic activity into the ileum, thereby allowing the detection of bleeding lesions located beyond the reach of push enteroscopy. Because of prolonged examination (7 hours), patient discomfort, need for additional endoscopy staff to perform the procedure, and inability to perform therapy, Sonde enteroscopy is rarely used in clinical practice.

**Push enteroscopy.** Video push enteroscopy is widely used in the diagnosis and management of obscure GI bleeding. Originally, adult or pediatric colonoscopes were used to examine the proximal small intestine; subsequently, dedicated push enteroscopes were developed with working lengths of 220–250 cm. Looping of the enteroscope in the stomach results in patient discomfort and limits the extent of the examination to 50–150 cm of proximal small bowel. Use of an overtube has been shown to prevent looping and improve the depth of insertion of a push enteroscope but without an impact on diagnostic yield.

The diagnostic yield of push enteroscopy in patients with obscure bleeding ranges from 3% to 70%. Angioectasias are the most common lesions, identified in 7%–60% of examinations (Table 3). In addition to the detection of lesions in the proximal small intestine, push enteroscopy allows diagnosis of lesions overlooked in the stomach and duodenum during prior upper endoscopy in 6%–37% of patients. Hence, it is important to carefully examine the stomach and duodenum, if necessary with a standard upper endoscope before the push enteroscopy, depending on the quality of the prior examination and experience of the endoscopist.

<table>
<thead>
<tr>
<th>Author, year (reference)</th>
<th>No. of patients with bleeding</th>
<th>Diagnostic yield (%)</th>
<th>Yearly recurrence (%)a</th>
<th>Mortality (%)</th>
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<tbody>
<tr>
<td>Desa et al, 1991</td>
<td>12</td>
<td>83</td>
<td>30</td>
<td>17</td>
</tr>
<tr>
<td>Resse et al, 1992</td>
<td>44</td>
<td>70</td>
<td>60</td>
<td>11</td>
</tr>
<tr>
<td>Lopez et al, 1996</td>
<td>16</td>
<td>88</td>
<td>12.5</td>
<td>0</td>
</tr>
<tr>
<td>Zaman et al, 1999</td>
<td>14</td>
<td>58</td>
<td>43</td>
<td>0</td>
</tr>
<tr>
<td>Douard et al, 2000</td>
<td>25</td>
<td>81</td>
<td>38</td>
<td>4</td>
</tr>
<tr>
<td>Kendrick et al, 2001</td>
<td>70</td>
<td>74</td>
<td>48</td>
<td>6</td>
</tr>
<tr>
<td>Hartmann et al, 2005</td>
<td>47</td>
<td>72</td>
<td>N/A</td>
<td>2</td>
</tr>
<tr>
<td>Jakobs et al, 2006</td>
<td>81</td>
<td>84</td>
<td>N/A</td>
<td>0</td>
</tr>
</tbody>
</table>

aCalculated from $p = 1 − e^{−rt}$, where $r$ represents rate and $t$ represents time.

**Capsule endoscopy.** An endoscopic capsule was initially developed to obtain images from the small bowel (Given Imaging Ltd, Yoqneam, Israel). The present small bowel capsules, which measure 11 × 26 mm, contain light-emitting diodes, a lens, a color camera chip, 2 batteries, a radiofrequency transmitter, and an antenna. Depending on the manufacturer, the camera can be a complementary metal oxide semiconductor chip or a charge-coupled device. The capsule obtains images and transmits the data via radiofrequency to a recording device worn about a patient’s waist. Once the acquisition time is reached, the recording device is downloaded to a computer workstation whose software provides the images to the computer screen. The capsule is disposable and does not need to be retrieved by the patient. It is passed naturally. In addition to the images, software is available to provide localization of the capsule based on signal strength to the skin sensors, and other algorithms can aid in the identification of blood or vascular lesions. Small bowel obstruction is a contraindication for capsule endoscopy. In patients with swallowing disorders, the capsule can be placed into the duodenum directly using a capsule-loading device. Small case series have suggested that capsule endoscopy is safe in patients with pacemakers and defibrillators, although patients should be carefully monitored during the capsule examination. The cost-effectiveness of the capsule endoscopy study in
the evaluation of patients with obscure GI bleeding may be increased by the preview of the recordings by an endoscopy nurse or an assistant.\textsuperscript{107–109}

In a pilot study by Appleyard et al in 2000, radio-opaque beads were sewn into canine small bowels to compare the diagnostic yield between push enteroscopy and capsule endoscopy. Capsule enteroscopy identified more beads overall (64%) compared with push enteroscopy (37%), although push enteroscopy was found to be more sensitive for bead detection in the first meter of the examination (94% compared with 53% for capsule).\textsuperscript{110} In a prospective comparative study, capsule endoscopy underestimated the number of small bowel polyps in persons with familial adenomatous polyposis compared with push enteroscopy.\textsuperscript{111} Therefore, negative findings on a capsule endoscopic examination do not exclude pathology in the small intestine. Because lesions limited to 3–4 frames may be easily missed, it is important to review the capsule endoscopy at a slower frame rate to detect subtle lesions.\textsuperscript{112}

Published experience has shown that capsule endoscopy identifies causes of blood loss in the small bowel twice as often as push enteroscopy. There have been 10 published studies comparing capsule endoscopy with

![Table 3. Selected Studies Using Push Enteroscopy for Obscure GI Bleeding](image)

<table>
<thead>
<tr>
<th>Author, year (reference)</th>
<th>No. of patients and type of bleeding</th>
<th>Diagnostic yield (%)</th>
<th>Examinations with angiectasias (%)</th>
<th>Endoscopic therapy (%)</th>
<th>Bleeding cessation per year/patients with angiectasias (%)\textsuperscript{a}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Foutch et al, 1990\textsuperscript{84}</td>
<td>20 overt, 19 occult</td>
<td>15 (38)</td>
<td>31</td>
<td>92</td>
<td>44</td>
</tr>
<tr>
<td>Chong et al, 1994\textsuperscript{15}</td>
<td>55 overt</td>
<td>35 (64)</td>
<td>4</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Pennazio et al, 1995\textsuperscript{14}</td>
<td>21 overt</td>
<td>9 (43)</td>
<td>38</td>
<td>12.5</td>
<td>N/A</td>
</tr>
<tr>
<td>Davies et al, 1995\textsuperscript{16}</td>
<td>11 overt, 7 occult</td>
<td>6 (33)</td>
<td>11</td>
<td>100</td>
<td>N/A</td>
</tr>
<tr>
<td>Schmit et al, 1996\textsuperscript{18}</td>
<td>37 overt, 46 occult</td>
<td>49 (59)</td>
<td>40</td>
<td>42</td>
<td>38</td>
</tr>
<tr>
<td>Adrain et al, 1998\textsuperscript{85}</td>
<td>41 overt</td>
<td>32 (78)</td>
<td>49</td>
<td>N/A</td>
<td>27</td>
</tr>
<tr>
<td>Zaman et al, 1998\textsuperscript{6}</td>
<td>75 overt, 20 occult</td>
<td>39 (41)</td>
<td>46</td>
<td>61</td>
<td>60</td>
</tr>
<tr>
<td>Shackel et al, 1998\textsuperscript{190}</td>
<td>23 overt, 21 occult</td>
<td>23 (52)</td>
<td>65</td>
<td>73</td>
<td>40</td>
</tr>
<tr>
<td>Descamps et al, 1999\textsuperscript{17}</td>
<td>110 overt, 123 occult</td>
<td>125 (53)</td>
<td>63</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Hayat et al, 2000\textsuperscript{91}</td>
<td>50 occult, 28 overt</td>
<td>43 (78)</td>
<td>26</td>
<td>100</td>
<td>N/A</td>
</tr>
<tr>
<td>Sharma et al, 2000\textsuperscript{52}</td>
<td>21 overt, 5 occult</td>
<td>9 (43)</td>
<td>4.7</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Landi et al, 2002\textsuperscript{93}</td>
<td>49 overt, 56 occult</td>
<td>49 (47)</td>
<td>37</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Lewis et al, 2002\textsuperscript{94}</td>
<td>21 overt</td>
<td>6 (30)</td>
<td>30</td>
<td>100</td>
<td>N/A</td>
</tr>
<tr>
<td>Ell et al, 2002\textsuperscript{95}</td>
<td>32 overt</td>
<td>9 (32)</td>
<td>22</td>
<td>14</td>
<td>N/A</td>
</tr>
<tr>
<td>Mylonaki et al, 2003\textsuperscript{96}</td>
<td>50 overt</td>
<td>16 (32)</td>
<td>20</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Saurin et al, 2003\textsuperscript{52}</td>
<td>28 overt, 32 occult</td>
<td>3 (3)</td>
<td>7</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Keizman et al, 2003\textsuperscript{97}</td>
<td>36 overt, 57 occult</td>
<td>51 (40)</td>
<td>35</td>
<td>100</td>
<td>85</td>
</tr>
<tr>
<td>Romelaer et al, 2004\textsuperscript{98}</td>
<td>66 overt, 53 occult</td>
<td>50 (42)</td>
<td>66</td>
<td>76</td>
<td>76</td>
</tr>
<tr>
<td>Adler et al, 2004\textsuperscript{99}</td>
<td>20 occult</td>
<td>5 (25)</td>
<td>10</td>
<td>100</td>
<td>60</td>
</tr>
<tr>
<td>Mata et al, 2004\textsuperscript{100}</td>
<td>26 overt, 16 occult</td>
<td>8 (19)</td>
<td>9.5</td>
<td>50</td>
<td>N/A</td>
</tr>
<tr>
<td>Pennazio et al, 2004\textsuperscript{101}</td>
<td>34 overt, 17 occult</td>
<td>15 (29)</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>Lara et al, 2005\textsuperscript{102}</td>
<td>44 overt, 19 occult</td>
<td>35 (56)</td>
<td>30</td>
<td>100</td>
<td>N/A</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>N/A, not available.</th>
</tr>
</thead>
</table>

\textsuperscript{a}Calculated from $p = 1 - e^{-rt}$, where $r$ represents rate and $t$ represents time.

| Table 4. Push Enteroscopy Compared With Capsule Endoscopy |

<table>
<thead>
<tr>
<th>Author, year (reference)</th>
<th>No. of patients and type of bleeding</th>
<th>Push enteroscopy positive (%)</th>
<th>Capsule endoscopy positive (%)</th>
<th>Findings on both push enteroscopy and capsule endoscopy (%)</th>
<th>Additional capsule yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lewis and Swain, 2002\textsuperscript{84}</td>
<td>21 overt</td>
<td>6 (30)</td>
<td>11 (55)</td>
<td>6 (30)</td>
<td>25</td>
</tr>
<tr>
<td>Eli et al, 2002\textsuperscript{95}</td>
<td>32 overt</td>
<td>9 (28)</td>
<td>21 (66)</td>
<td>6 (19)</td>
<td>38</td>
</tr>
<tr>
<td>Mylonaki et al, 2003\textsuperscript{96}</td>
<td>50 overt</td>
<td>16 (32)</td>
<td>38 (76)</td>
<td>N/A</td>
<td>44</td>
</tr>
<tr>
<td>Saurin et al, 2003\textsuperscript{95}</td>
<td>28 overt, 32 occult</td>
<td>3 (3)</td>
<td>21 (35)</td>
<td>19 (32)</td>
<td>32</td>
</tr>
<tr>
<td>Hartmann et al, 2003\textsuperscript{113}</td>
<td>33 overt</td>
<td>7 (21)</td>
<td>25 (76)</td>
<td>31 (94)</td>
<td>55</td>
</tr>
<tr>
<td>Adler et al, 2004\textsuperscript{99}</td>
<td>20 occult</td>
<td>5 (25)</td>
<td>14 (70)</td>
<td>N/A</td>
<td>45</td>
</tr>
<tr>
<td>Mata et al, 2004\textsuperscript{100}</td>
<td>26 overt, 16 occult</td>
<td>8 (19)</td>
<td>31 (74)</td>
<td>8 (19)</td>
<td>55</td>
</tr>
<tr>
<td>Ge et al, 2004\textsuperscript{184}</td>
<td>32 overt</td>
<td>9 (25)</td>
<td>21 (66)</td>
<td>9 (25)</td>
<td>41</td>
</tr>
<tr>
<td>Pennazio et al, 2004\textsuperscript{101}</td>
<td>34 overt, 17 occult</td>
<td>15 (29)</td>
<td>30 (59)</td>
<td>12 (24)</td>
<td>30</td>
</tr>
<tr>
<td>Neu et al, 2005\textsuperscript{185}</td>
<td>37 overt, 19 occult</td>
<td>15 (38)</td>
<td>38 (68)</td>
<td>N/A</td>
<td>30</td>
</tr>
<tr>
<td>Totals</td>
<td>397</td>
<td>93 (23)</td>
<td>250 (63)</td>
<td>39.5</td>
<td></td>
</tr>
</tbody>
</table>

| N/A, not available. |
push enteroscopy in the evaluation of patients with obscure GI bleeding. All 10 studies were prospective, and 7 were blinded. Together, these reports show a 63% (250/397) yield for capsule endoscopy and a 23% (93/397) yield for push enteroscopy. A pooled analysis of raw data from manufacturer-sponsored trials showed that capsule endoscopy has a significantly increased capability to detect pathology as compared with push enteroscopy, small bowel series, and colonoscopy with ileal intubation. Capsule endoscopy identified pathology in approximately 70% of the examinations in the pooled data analysis of 530 capsule examinations. This was double the yield of other methods. Approximately 90% of 1349 pathologies were not identified by any other method other than capsule endoscopy. A metaanalysis of both published trials and abstracts also attests to this increased yield. A total of 14 studies comparing capsule endoscopy with push enteroscopy were reviewed, with a combined yield of 63% for capsule endoscopy and 28% for push enteroscopy.

The validity of the findings made by capsule endoscopy was confirmed by a prospective study comparing capsule endoscopy with what has been considered the gold standard in small bowel visualization, intraoperative endoscopy, in 47 patients. The overall yield for capsule endoscopy was 74%, and the overall yield for both procedures was 76.6%. Bleeding sites were identified by both techniques in 36, by capsule only in 2, and by intraoperative enteroscopy only in 1. The findings of both examinations were negative in 11. The calculated sensitivity for capsule endoscopy was 95%, specificity was 75%, and positive and negative predictive values were 95% and 86%, respectively.

Long-term follow-up studies have allowed calculation of sensitivity and specificity for capsule endoscopy by obtaining a final diagnosis during the follow-up period. Pennazio et al reported a 1-year follow-up of 100 patients with obscure bleeding. Sensitivity, specificity, and positive and negative predictive values of capsule endoscopy were 89%, 95%, 97%, and 83%, respectively, in the 56 patients in whom a definite confirmed diagnosis was obtained. Delvaux et al reported a 1-year follow-up experience in 44 patients. The positive predictive value of capsule endoscopy was 94.4% in those with findings at capsule endoscopy, and the negative predictive value was 100% in patients with normal findings on capsule examination.

In addition to the ability of capsule endoscopy to make more diagnoses with accuracy, its therapeutic impact has begun to be measured. Kraus et al reported that in 33% of cases, findings on capsule examination guided additional diagnostic and therapeutic steps. Ben Soussan et al reported that in 37% of examinations, new steps in management were undertaken, including endoscopic management in 10, surgery in 2, and medical therapy in 1. Mylonaki et al reported that capsule endoscopy led to an alteration of therapy in 66% of patients with positive findings. Pennazio et al reported that in 20 of 23 patients in who capsule endoscopy was performed for ongoing overt bleeding, directed treatments led to resolution of bleeding in 87%. Overall, follow-up data on 91 patients during a mean follow-up period of 18 months showed that subsequent management dictated by capsule endoscopy led to the resolution of bleeding in 59 (65%). There is a lack of other published data concerning outcomes following capsule endoscopy and subsequent interventions. There are no published data to date on the rate of continued bleeding or further testing initiated. In addition, the recurrence of angiectasias after endoscopic therapy is currently unknown.

Investigators have looked at patient selection for capsule endoscopy to determine if this influences the yield of the examination. Bresci et al reported a greater yield for capsule endoscopy (91% vs 34%) if capsule endoscopy were performed within 2 weeks of a bleeding episode. May et al reported that patient selection for capsule endoscopy also affected yields. Patients who had been enrolled in a study of capsule endoscopy in which inclusion criteria included a decrease in hemoglobin level less than 10 g, anemia, or bleeding persisting for more than 6 months and the occurrence of more than 1 bleeding episode were more likely to have a source of bleeding identified. None of the patients who had a minimum hemoglobin value $\geq$ 10 g/dL had a positive capsule result.

Provocation of bleeding using anticoagulation may increase the detection of lesions during capsule endoscopy, as reported in 2 cases recently. Despite extensive literature concerning the effectiveness of this technology, most overlook the importance and intensity of examining the obtained images. Typical examinations obtain images over 8 hours. Because images are obtained at a rate of 2 images per second, a total of 57,600 images are produced. The computer workstation allows images to be viewed singly or as a video stream. Although obtained at 2 images/second, images may be reviewed up to 40 images/second. Because an abnormality may be present on only one image, most physicians familiar with the system believe that lesions could easily be missed at the faster rates. A single image is only on the monitor for less than 2/100th of a second when viewing at 40 images/second. A consensus conference of users in 2002 agreed that 15 frames/second is the fastest acceptable rate of review. At this rate, 57,600 images can be seen in 64 minutes. This only takes into account running the images as a video without stopping to examine individual images. Lewis and Swain reported the viewing times of 20 examinations performed using the Given system (Given Imaging Ltd). They averaged 56 minutes to review only the small bowel images, with a range of 34–94 minutes. Ell et al also reported taking an average of 50 minutes in examining the small bowel data of 32 patients. The range was from 30 to 120
minutes. Costamagna et al reported taking 2 hours to review each study. It was unclear in this study if the images reviewed included the gastric and colonic portions. In an effort to shorten the review time, software has been developed to allow the reader to view 2 or 4 images simultaneously. Dual image reading places 2 images, one full second of image collection, on one screen, side by side, while a quad view places 4 images or 2 seconds of imaging on each screen. This could theoretically shorten the reading time by as much as 50%. In addition to the length of time the review takes, physicians are also concerned about reading the studies properly and not missing lesions. To aid physicians in this regard, software has been added to the system to identify red pixels as suspected bleeding areas.

In addition to vigilance, physicians must have experience in interpreting endoscopic images. Only one part of capsule endoscopy is the vigilant reader, who is able to identify an area that is different or abnormal from other areas examined. An equally important part of the examination is the proper identification of these abnormalities. The reader must be able to make a diagnosis based on the images. This will allow the dismissal of normal variants and nonpathologic lesions and the identification of specific pathologies requiring specific therapies. The images obtained at capsule endoscopy are slightly different from traditional endoscopy because there is no air distention of the bowel wall and the capsule is at times located within millimeters of the mucosa. This is so-called "physiologic endoscopy." The bowel is not altered by the process of the examination. There is no sedation used, and thus there are no hemodynamic effects. There is no trauma caused by the capsule. There is no air insufflation to affect the microvasculature. Thus, all findings are real and their location has not been altered by the examination. Expertise must be obtained to allow review of the images not only in an efficient manner but also to provide a precise diagnosis.

There are specific problems when interpreting some capsule images. These include single image abnormalities, proper identification of submucosal processes, and differentiating dark blood from dark bile. Unlike traditional endoscopy, a single image abnormality cannot be viewed from different angles but rather must be identified by a single 0.5-second image. This is dependent on experience and confidence of the reader. Equally troubling, a submucosal lesion can be mistaken for the bulge created by another loop of bowel overlying the loop being inspected. There are visual cues that allow for this differentiation. The presence of bridging folds speaks to a submucosal process. Capsule images can also clearly show the stretching of the mucosa as well as mucosal edema. Conversely, overlying loops can be suspected when the indentation moves with peristalsis, indicating its softness. Bubbles from bile could interfere with the capsule endoscopic examination, which could be avoided with the use of simethicone before the examination. Dark bile is another situation that can be difficult to interpret because it can be mistaken for dark blood. This is avoided by examining the mucosa beyond the stained area to see if coffee ground or bloody material is seen. Its absence indicates likely bile proximally. Endoscopically evident small intestinal mucosal injury is very common among chronic NSAID users, which can complicate the interpretation of images in arriving at a final diagnosis.

Patients with ongoing hospitalization may be at risk of retention of the capsule in the stomach for a prolonged period. This could be prevented by the use of prokinetics before capsule ingestion or endoscopic delivery of the capsule in patients with gastric outlet obstruction. Although small intestinal capsule retention has not been reported in normal subjects or those with diverticulosis, capsule retention can occur in less than 1% of patients due to localized pathology. Sources of bleeding can be localized in all the cases with capsule retention in the small intestine. A history of NSAID use may be associated with an increased risk of capsule retention. Although the majority of patients with capsule retention are asymptomatic, complications such as aspiration, retention in Zenker’s diverticulum, intestinal perforation, and obstruction have been reported. Retained capsules may be removed by endoscopy or surgery. Patients should not undergo magnetic resonance imaging until they have passed the capsule, which can be easily confirmed by a plain radiograph if necessary.

The International Conference on Capsule Endoscopy produced a consensus statement on obscure GI bleeding. Their conclusion was as follows:

Capsule endoscopy is currently the preferred test for mucosal imaging of the entire small intestine and should be part of the initial investigation in patients with obscure bleeding. Its diagnostic yield is high and potentially it can produce earlier diagnosis. When integrated into a global approach to the patient, capsule endoscopy is helpful in achieving effective decision-making concerning subsequent investigations and treatments. This in turn could mean more timely treatment and lower overall utilization and cost. Large prospective studies are however necessary to better assess the impact of capsule endoscopy on clinical outcomes.

DBE. DBE, first described by Yamamoto et al in 2001, allows complete visualization of the small intestine using a 200-cm enteroscope with an OD of 8.5 mm equipped with a 140-cm overtube with an OD of 12 mm (Fujinon Inc, Saitama, Japan). Latex balloons at the tip of the enteroscope and the overtube are inflated and deflated with air from a pressure-controlled pump system. By inflating the overtube balloon enough to grip the intestinal wall (which can occur at a balloon pressure of 45 mm Hg), the enteroscope can be inserted further without forming redundant loops in the small intestine. The overtube can then be inserted while the endoscope balloon is inflated. This method allows for insertion of the
endoscope deep into the small intestine and is also known as “push-and-pull enteroscopy.”

To estimate the mean depth of insertion during a DBE examination, 2 methods have been proposed. In the first method, which has been the most commonly used, the length of endoscope advancement in each round of the push-pull cycle is added; the distance lost if slippage occurred is estimated and subtracted to calculate a metric measure of the length of the small bowel examined. Using this method, the mean (SD) distance achieved was 240 (100) cm during the antegrade approach and 140 (90) cm for the retrograde approach in the study by May et al, with mean examination times of 72.5 (23) and 75 (28) minutes, respectively. In the US multicenter trial, the estimated depths of insertion were 360 (178) cm for the oral DBE examinations with a mean examination time of 95 (41) minutes and 182 (165) cm for the retrograde DBE examinations with a mean examination time of 102 (38) minutes. In the second method, information from contrast injection during fluoroscopy and position of the tip of the DBE scope was used to estimate the farthest reach of the endoscope. Per-oral examinations achieved a mean distance of 360 (177) cm from the pylorus in the 4 centers in the US multicenter study.

Except for rare instances, complete small bowel enteroscopy with cecal intubation by the antegrade approach alone is not feasible. In addition, total enteroscopy, defined as initial DBE from one approach with India ink tattooing using a sclerotherapy needle at the furthest insertion point followed by DBE from opposite direction with prior tattoo site identified, is not necessary.

### Table 5. Yield of DBE in Patients With Obsolete GI Bleeding

<table>
<thead>
<tr>
<th>Author, year (reference)</th>
<th>Patients with bleeding a/DBE examinations (%)</th>
<th>Diagnostic yield (%)</th>
<th>Diagnostic or treatment success (%)</th>
<th>Total DBE (%) b</th>
<th>Rebleed rate (%)</th>
<th>Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yamamoto et al, 2004142</td>
<td>66/178 (37)</td>
<td>76</td>
<td>61</td>
<td>86</td>
<td>N/A</td>
<td>Perforation, 1 (0.6)</td>
</tr>
<tr>
<td>May et al, 2005140</td>
<td>90/248 (36)</td>
<td>80</td>
<td>76</td>
<td>45</td>
<td>N/A</td>
<td>None</td>
</tr>
<tr>
<td>Ell et al, 2005144</td>
<td>64/147 (44)</td>
<td>72</td>
<td>62</td>
<td>16</td>
<td>N/A</td>
<td>None</td>
</tr>
<tr>
<td>Di Caro et al, 2005145</td>
<td>33/89 (37)</td>
<td>80</td>
<td>42</td>
<td>44</td>
<td>N/A</td>
<td>None</td>
</tr>
<tr>
<td>Matsumoto et al, 2005151</td>
<td>13/22 (59)</td>
<td>46</td>
<td>N/A</td>
<td>14</td>
<td>N/A</td>
<td>None</td>
</tr>
<tr>
<td>Meh dizadeh et al, 2006141</td>
<td>130/237 (55)</td>
<td>43</td>
<td>60</td>
<td>0</td>
<td>N/A</td>
<td>Perforation, 1 (0.4)</td>
</tr>
<tr>
<td>Hadithi et al, 2006146</td>
<td>35/35 (100)</td>
<td>60</td>
<td>77</td>
<td>20</td>
<td>20</td>
<td>None</td>
</tr>
<tr>
<td>Heine et al, 2006147</td>
<td>168/275 (61)</td>
<td>73</td>
<td>55</td>
<td>42</td>
<td>N/A</td>
<td>Perforation, 1 (2.5) Pancreatitis, 3 (1)</td>
</tr>
<tr>
<td>Kaffes et al, 2006148</td>
<td>32/40 (80)</td>
<td>48</td>
<td>75</td>
<td>0</td>
<td>N/A</td>
<td>Perforation, 1 (1.4) Polypectomy bleed, 1 (3.6)</td>
</tr>
<tr>
<td>Mon kemuller et al, 2006149</td>
<td>29/70 (41)</td>
<td>67</td>
<td>57</td>
<td>30</td>
<td>0</td>
<td>None</td>
</tr>
<tr>
<td>Nakamura et al, 2006150</td>
<td>32/28 (100)</td>
<td>41</td>
<td>43</td>
<td>62.5</td>
<td>6</td>
<td>Perforation, 1 (3.6)</td>
</tr>
<tr>
<td>Manabe et al, 2006152</td>
<td>31/31 (100)</td>
<td>74</td>
<td>74</td>
<td>29</td>
<td>91</td>
<td>None</td>
</tr>
<tr>
<td>Totals</td>
<td>723 patients, 1400 examinations</td>
<td>65</td>
<td>64</td>
<td>29</td>
<td>91</td>
<td>None</td>
</tr>
</tbody>
</table>

N/A, not available.

aIncludes patients with obscure overt and/or obscure occult bleeding.
bDefined as initial DBE from one approach with tattoo at most distal insertion point followed by DBE from opposite direction with prior tattoo site identified.
No specific preparation is required for the oral approach, while bowel cleansing is required for the anal approach. Although many centers have performed the procedure using general anesthesia, the procedure can be safely performed under conscious sedation. DBE via the anal approach can be challenging due to bowing of the floppy enteroscope and difficulty in maintaining the enteroscope proximal to the ileocecal valve for successful ileal intubation. In addition, poor colon preparation limits advancement through the colon, and adhesions from previous surgery or radiation may limit endoscope insertion. The failure rate of the anal approach and retrograde ileal intubation varies from 5% to 30%. The learning curve for retrograde DBE examinations appears to be steep but has not been quantified. Successful reduction of colonic loops starting early during the procedure and continuing until entrance into the ileocecal valve and keeping a relatively straight position of the endoscope may improve the ileal intubation rate. Introduction of a stiffer double-balloon therapeutic enteroscope did not improve ileal intubation rates. Recently, a balloon-assisted technique has been proposed as an aid for ileal intubation.

DBE is safe. There are no deaths reported to date, and the morbidity is low. Intestinal perforation occurred in 4 of 1378 procedures (0.3%); one patient with intestinal lymphoma undergoing chemotherapy, another patient with a recent laparotomy who sustained a peristomal tisis, a third patient after cautery of an angiectasia, and a fourth patient with a duodenal perforation. Mild pancreatitis possibly due to duodenal hypertension from double-balloon inflation was reported in 3 patients. Prolonged ileus lasting for 4 days was reported in a patient after DBE.

Training in the use of DBE can be accomplished by observation of live cases followed by hands-on training using porcine specimens on the Erlangen Endo-Trainer. The European experience of DBE hands-on training of 97 participants in 13 workshops using the Erlangen Endo-Trainer is encouraging. The evaluation of the depth of measurement method during the workshops using the 100-cm and 200-cm insertion points showed that the estimation of the insertion depths was accurate, with a mean deviation of <10%. Such a training program might be useful in providing training to US gastroenterologists. Fluoroscopy is useful during the early training period to guide endoscope passage, confirm final endoscope tip position, and monitor and reduce any looping of the enteroscope that may occur during the procedure. After the first 10 cases of DBE, both the procedural time (109 ± 44.6 minutes initially and 92.4 ± 37.6 minutes after 10 cases; P = .005) and the use of fluoroscopy decreases significantly. Although there is no significant change in the anal DBE procedure time, the antegrade examination time decreases significantly after the first 7 cases (P = .003).

Based on the current published data on DBEs, 723 patients have undergone 1400 DBE examinations with an average diagnostic yield of 65% and diagnostic or treatment success of 64%. Observe bleeding was the indication for DBE in approximately 36%–100% of examinations, and the overall diagnostic yield from DBE ranged from 43% to 80%. Diagnostic or therapeutic success was reached in 55%–75% of examinations, which is comparable to other diagnostic modalities for the small bowel. Patients with obscure bleeding as an indication for DBE have a higher success rate. Data regarding rebleeding rates after endoscopic or other therapy for angiectasias are needed for DBE, as for all of the other endoscopic modalities.

In 8 of the 12 DBE studies published to date (Table 5), specific findings were detailed for 488 patients presenting with obscure bleeding. In total, angiectasias were found in 153 (31%) of examinations (range, 6%–55%), ulcerations (including inflammatory bowel disease) in 66 patients (13%; range, 2%–35%), malignancies in 40 patients (8%; range, 3%–26%), other etiologies (including small bowel diverticula) in approximately 28 (6%; range, 2%–22%), and no findings in 198 patients (40%; range, 0–57%). In the study by Manabe et al, 91% of the patients treated endoscopically or surgically for a bleeding source did not have any further bleeding over a mean of 8.5 ± 0.6 months (range, 4–14 months).

Three studies to date have compared capsule endoscopy with DBE for patients with obscure GI bleeding. In all 3 studies, the yield for capsule endoscopy was higher than that for DBE. The reasons for the higher yield on capsule endoscopy include complete visualization of the small bowel and potential false-positive lesions that are not confirmed on DBE, including nonspecific “red spots.” The agreement between capsule endoscopy and DBE has ranged between 61% and 74%. In the US multicenter trial, the agreement was calculated to be 74% for angiectasias, 96% for ulcerations, 94% for mucosal and submucosal polyps, and 96% for large tumors. Using the κ statistic, the agreement for 115 patients who underwent both capsule endoscopy and DBE was substantial for ulcers and large masses (0.74 and 0.59, respectively) but only moderate for angiectasias (0.42) and poor for mucosal polyps (0.2), potentially due to false readings of mucosal bulges on the capsule endoscopy examinations. The calculated miss rates were 28% for DBE and 20% for capsule endoscopy. In another study examining 13 patients with GI bleeding and 9 patients with polyposis, patients were examined by DBE followed by capsule endoscopy within 1 week. Patients who had a positive capsule endoscopy underwent a repeat DBE from the opposite approach. In the patients with obscure bleeding the agreement was 92%, whereas the yield in patients with polyposis was 67% for DBE compared with 33% for capsule endoscopy. More com-
parative studies are warranted for the 2 diagnostic modalities in patients with obscure bleeding.

In summary, DBE appears to have superior diagnostic capability compared with push enteroscopy and equivalent yield compared with intraoperative enteroscopy without the associated morbidity of the latter procedure. While DBE does not allow visualization of the entire small bowel in one examination compared with capsule endoscopy, it has been shown to be associated with an equivalent detection rate, has the capability to detect lesions missed by capsule endoscopy, and offers the advantages of therapeutic treatment. With the advent of DBE, intraoperative enteroscopy can be relegated to the archives of diagnostic procedures along with Sonde enteroscopy, except for cases where the success of DBE is limited by the presence of adhesions or other anatomic factors.

A single-balloon enteroscopy is currently undergoing evaluation and will be released into the market soon.

Cost

The current medical literature lacks sufficient information concerning the costs associated with diagnosing obscure GI bleeding. The most comprehensive review of the economic literature for the period from 1985 to 1995 has limited information of value in understanding the costs and was not limited to obscure bleeding.157

There are various issues that contribute to the medical costs incurred in these patients. It may take considerable time to diagnose a patient with obscure bleeding. The median time to diagnose patients with obscure bleeding has been estimated as 2 years, with a range from 1 month to 8 years. In addition to this extended time to diagnosis, patients undergo numerous diagnostic tests and evaluations before a bleeding source is identified. Foutch et al reported that 39 patients undergoing push enteroscopy for unidentified obscure bleeding had a total of 277 diagnostic tests performed before study entry.84 This was an average of 7.3 tests per patient. In this study, 49% of the patients continued to have an unknown bleeding source after push enteroscopy. The difficulties in locating the bleeding site with currently available diagnostic tools often result in the need for repeat testing, thus increasing the economic burden of obscure bleeding. In addition, patients with obscure bleeding may require blood transfusions and repeated hospitalizations. Flickinger et al reported 14 patients with obscure bleeding who had an average of 5 hospital admissions and an average of 46 units of blood transfused before undergoing intraoperative enteroscopy.158

In an attempt to calculate the cost of obscure GI bleeding, Goldfarb et al reported costs incurred in 21 patients with obscure bleeding.159 The mean length of time from first recognition of bleeding to study entry was 2.7 years. One patient who had gone 12 years since first bleed was excluded in this calculation. Because actual cost and charge data were not available, costs from a payer reimbursement perspective were based on average Medicare fees. For example, for hospitalizations, the average Medicare reimbursement for DRG 174 (GI hemorrhage with complications or comorbid conditions) is $4264. Commercial reimbursements would be significantly higher. Transfusion costs were based on a prior economic analysis. The costs associated with diagnosing obscure bleeding and treating the anemia were significant, averaging $33,630 per patient without a diagnosis made in capsule study patients before entry. Furthermore, data on other utilizations contributing to direct medical costs, such as physician visits, emergency department visits, and prescriptions, were not collected as part of the trial. Therefore, it appears that these figures significantly underestimate the total cost of care and diagnosis of patients with obscure GI bleeding.

Recently, Kamal and Gerson published a cost-effectiveness analysis examining potential strategies for the diagnosis and management of bleeding small bowel angioectasias.160 The base-case patient for the analysis was a 70-year-old patient with obscure overt bleeding from small bowel angioectasias. The diagnostic and treatment alternatives in the model included (1) no therapy (reference arm); (2) push enteroscopy; (3) intraoperative enteroscopy; (4) angiography; (5) initial empirical DBE via the oral approach, followed by repeat DBE via the rectal approach if the oral examination was normal; and (6) small bowel capsule endoscopy followed by DBE using the approach dictated by capsule findings. Cost estimates were obtained from a third-party payer perspective. Primary outcome measures were number of patients with cessation of bleeding, average cost per patient, and procedural complications. Patients in the reference arm or with unsuccessful treatment were assumed to have ongoing transfusion requirements of 2 units/month.

The results of the model demonstrated that capsule-directed DBE and the initial DBE strategy were equally effective, but the initial DBE arm was less expensive and was the most cost-effective approach with an incremental cost-effectiveness ratio of $1653 per patient successfully treated. Assuming a cohort of 1000 patients with obscure bleeding from small bowel angioectasias, approximately 741/1000 (74%) would have cessation of bleeding in the DBE arm over the course of 1 year with a per-patient cost of $1717 compared with a 40% bleeding cessation rate at a cost of $1171 per patient for the no therapy arm. Sensitivity analyses demonstrated that capsule-directed DBE would be the preferred approach if there was a probability of 85% or greater that an angioectasia would be detected on capsule endoscopy and a probability of 62% or less that an angioectasia would be detected on DBE. Angiography would be the preferred approach if the probability of finding a lesion on angiography exceeded 85%, if the success rate associated with DBE was 64% or less, or if the probability of finding an angioecta-
sias on DBE was 35% or less. Intraoperative enteroscopy was preferred if the success rate after treatment exceeded 80%. The investigators concluded that for patients with obscure occult bleeding from small bowel angiectasias, initial DBE is a cost-effective approach. More research examining the ideal strategies for patients with obscure bleeding and the effect of obscure bleeding on health-related quality of life is warranted.

**Management**

The American Gastroenterological Association medical position statement concerning the evaluation and management of obscure GI bleeding was published in January 2000, before the initial studies utilizing capsule endoscopy and DBE. The position statement proposes progressive testing with bleeding scans and angiography for those patients with active bleeding, as well as repeat endoscopy, enteroscopy, enteroclysis, or small bowel series for those not actively bleeding. With continued blood loss, intraoperative enteroscopy is suggested. This guideline is similar to the management of the 21 patients reported by Goldfarb et al. The costs of this type of management were at least $33,630 per patient without a diagnosis made. This paradigm of progressive testing has become obsolete with the availability of capsule endoscopy and DBE during the past 5 years.

The extent of the evaluation of the patient with obscure bleeding is dependent on 2 major factors: the extent of the bleeding and the age of the patient. Patients with occult blood in their stool but no associated anemia most likely do not require evaluation beyond colonoscopy unless upper tract symptoms are present. Certainly advanced testing beyond colonoscopy and upper endoscopy is not warranted in this group. Patients with an ongoing transfusion requirement need a full evaluation. The most common cause of obscure bleeding in this group is angiectasias, accounting for up to 80% of causes. These patients are typically older than 60 years. Small bowel tumors are the most common cause of obscure bleeding in patients younger than 50 years. Young patients should be handled differently than older patients. Management decisions in the older group are often quite difficult because the natural history of angiectasias is still not known. It is estimated that less than 10% of all patients with angiectasias will eventually bleed. Once lesions have bled, their tendency to rebleed is also not known. Although physicians are anxious to treat these lesions, it may be that as many as 50% will not rebleed.

In the patient presenting with obscure GI bleeding with either positive fecal occult blood testing and associated anemia or overt bleeding with melena or maroon blood per rectum, colonoscopy and upper endoscopy should be performed. If normal, both examinations should be repeated. Barium studies can be considered but should not replace endoscopic examinations. In the face of continued bleeding and initially negative findings on colonoscopy and upper endoscopy, repeated endoscopic examinations can be worthwhile. Repeated barium studies are not indicated. Once all the standard examinations are negative, the small bowel may be assumed to be the source of blood loss.

Worldwide experience suggests that capsule endoscopy is the preferred method of small bowel evaluation due to the length of the small bowel examined, the quality of the examination, and the noninvasive nature of the test. Capsule endoscopy should be the third test in the evaluation of patients with GI bleeding, once findings on upper endoscopy and colonoscopy are negative. In the patient with active bleeding, capsule endoscopy can confirm the small bowel as the site of bleeding, providing a location. Even if the study findings are negative for the small bowel in the actively bleeding patient, the study may indicate that the bleeding is actually colonic or even gastric in origin. In the patient with active bleeding within the small intestine, the capsule will guide further evaluation and therapy. A patient with a small bowel tumor detected by capsule endoscopy will proceed directly to laparoscopic surgery. If the site of bleeding is identified in the proximal small bowel and there is no mass, push enteroscopy will be used to reidentify the site and cauterize the lesion. In cases where a distal small bowel site is identified, surgical intervention coupled with intraoperative enteroscopy or DBE will be necessary. Because the entire small bowel has been examined with the capsule examination, both examinations can be targeted and for surgery a laparoscopic-assisted approach coupled with intraoperative enteroscopy would only examine the suspected area. In patients with isolated iron deficiency or a more occult or intermittent type of bleeding, capsule endoscopy should be used similarly to identify an intestinal bleeding lesion and thereby direct subsequent testing or treatment. The early diagnosis of tumors of the small bowel will be obtained, and those with negative examinations will be reassured. Given the possibility of overlooked lesions on capsule endoscopy, it is critical to follow up the patients carefully and, if necessary, either a repeat examination with a capsule endoscope or enteroscopy should be considered. Although outcomes studies are needed, it would appear that the early use of capsule endoscopy would not only allow more rapid diagnosis and thus improved patient care but could also lessen the costs associated with obscure bleeding. Repeated colonoscopy and upper endoscopy would be avoided and, with a diagnosis, repeat hospitalizations and transfusions could be averted.

The major difficulty that will remain in the future is the patient with diffuse vascular lesions of the bowel or the patient with a distal lesion who cannot tolerate or will not permit surgical intervention. Fortunately, such patients are quite uncommon. Berner et al reported the results of enteroscopy in 450 patients with obscure bleeding. Only 4 patients had vascular lesions in the stomach, duodenum, jejunum, and ileum. Diffuse illness of
the bowel may suggest the presence of a systemic illness such as HHT or cirrhosis. Medical therapy of vascular lesions is contrary to general present practice. Endoscopic or surgical therapy is considered best at present due to its ease, relatively good long-term results, and the lack of a clearly effective, well-tolerated medical therapy (Figure 1).

The natural history of vascular lesions in the small bowel has not been well characterized. On close review of the placebo-controlled trials of hormonal therapy in the management of angiectasias of the GI tract, the spontaneous bleeding cessation rate in these patients varies from 40% to 50% per year. For example, in a 1992 study by Lewis et al, 44% of 34 untreated patients with small bowel angiectasias did not receive any transfusions over a mean follow-up period of 13.4 months (calculated spontaneous cessation rate of 38% per year). Recurrent bleeding occurs in about one third of patients who undergo investigation by push enteroscopy for GI bleeding of obscure origin, with a trend toward more frequent rebleeding in patients with angioectasias. Frequent previous bleeding episodes and transfusion requirements are predictive of recurrent bleeding. Findings on capsule endoscopy may assist in the follow-up evaluation of patients with obscure GI bleeding. In a recent study of 49 consecutive patients with obscure GI bleeding followed up for 19 months (range, 12–31 months), 48% of patients with positive findings on capsule endoscopy experienced rebleeding on long-term follow-up, compared with 5.6% of patients with negative findings on capsule endoscopy. Further invasive investigations can be deferred in patients with obscure GI bleeding and negative findings on capsule endoscopy.

Medical Management

The initial medical management of patients with overt brisk GI hemorrhage of an obscure source is similar to that of acute GI hemorrhage. Resuscitation takes priority over diagnostic workup, and many of these patients require inpatient management, including blood transfusion. Decisions regarding blood transfusion should be based on the patient’s clinical status, assessment of volume depletion, rate of bleeding, age, and other comorbid conditions. If the patient is on anticoagulation or platelet inhibitors, then consideration should be given on an individualized basis for withholding these drugs or even reversing their adverse effect on hemostasis.

Most patients with slow or intermittent obscure or occult GI bleeding will have coexistent iron deficiency anemia, which requires active management. The aim of the treatment should be to restore hemoglobin levels and mean corpuscular volume to normal and also replenish body stores. Laboratory measurements of body iron stores such as serum ferritin are helpful to assess the effectiveness of iron supplementation. This is achieved most easily with oral iron supplementation. Numerous oral iron preparations are available, although ferrous sulfate and ferrous gluconate are preferred forms of oral iron because of low cost and high bioavailability. A liquid preparation often is tolerated better. Ascorbic acid enhances iron absorption. Parenteral iron should only be used when there is intolerance to at least 2 oral iron preparations or noncompliance or when there is an element of iron malabsorption. Iron dextran was the only formulation approved for use in the United States until recently, when iron gluconate and iron sucrose were approved. The total required dose of iron can be administered as a single infusion using iron dextran; however, serious allergic reaction, including anaphylaxis, can occur in up to 10% of patients. With the other 2 iron salts for parenteral administration, anaphylaxis is less of a concern, but it usually takes multiple administrations to supplement the total dose.

Some patients with obscure GI bleeding are managed clinically with intermittent blood transfusions along with other nonspecific supportive measures such as avoidance of aspirin and anticoagulants as well as oral iron supplementation. These patients often do not have a definite diagnosis despite extensive workup, have diffuse GI angiectasias often in inaccessible locations, have failed endoscopic or surgical or other specific therapies, or are elderly with many comorbid conditions in whom the risk of further diagnostic evaluation is considered to be greater than the risk of nonspecific management. Although older reports suggest that nonspecific measures are often sufficient to maintain status quo, there is very little recent published information on the natural history and long-term prognosis of these patients.

**Pharmacologic Therapy**

Pharmacotherapy should be considered whenever endoscopic therapy, surgical intervention, or an-
giographic therapy is not practical or ineffective, such as patients in whom the source and the etiology of bleeding is unknown or the pathology is too diffuse to be amenable to ablative therapies.

The role of hormonal therapy continues to be most debated. Extrapolating clinical observation of beneficial effects of hormonal therapy in patients with HHT and nasal bleeding, hormonal therapy (eg, ethinyl estradiol and norethisterone) has been used for GI angiectasias. In a recent randomized placebo-controlled trial, 72 consecutive patients with acute and chronic bleeding due to gastroduodenal, colonic, and diffuse angiectasias were treated with ethinyl estradiol and norethisterone. Patients with HHT and those with cirrhosis were excluded. The primary end point was failure to prevent recurrent bleeding, either an acute episode or recurrent iron deficiency anemia despite persistent iron therapy. The results were uniformly negative for a beneficial effect of hormonal therapy, irrespective of disease site. Treatment failed in 39% of the treated patients and 46% of the placebo group, with similar rebleeding rates and transfusion requirements during a follow-up of up to 2 years. The actuarial chance of remaining free from bleeding after 2 years was 55% (95% confidence interval, 36%–74%) for the treatment group and 36% (14%–58%) for the placebo group (log-rank test; P = .649). Rebleeding was more likely to occur among patients with a previous history of multiple bleeds and in patients with chronic renal failure. However, the findings of the study do not apply to patients with HHT and those with chronic liver diseases, which was a frequent association, and the study was underpowered to identify a beneficial effect in patients with chronic renal failure. Also, the study patients had somewhat milder disease and did not receive concomitant or prior endoscopic therapy. Therefore, these disappointing results may not be applicable to all patients, in particular those with severe disease and who have failed endoscopic interventions. On the other hand, opponents of hormonal therapy commonly cite the increasing evidence of side effects, particularly cardiovascular, in patients on chronic hormonal therapy. It appears that appropriately powered controlled trials of hormonal therapy that include patients with severe disease and who have not responded to endoscopic therapy alone will be needed with long-term follow-up to answer these persistent issues.

Somatostatin and its analogue octreotide have been anecdotally reported to be beneficial in patients with obscure GI bleeding from angiectasias and blue rubber bleb nevus syndrome, possibly due to their inhibitory effect on angiogenesis and splanchnic blood flow. Recent case reports of a beneficial effect of thalidomide and its antiangiogenic effects in patients with obscure GI bleeding due to angiectasias and HHT have been reported. In a recent case report, erythropoietin was believed to stop chronic diffuse hemorrhage from GI mucosa; the exact mechanism is not known but may be related to the complex effect of erythropoietin on the platelet-subendothelial interactions and also on protein C, protein S, and anti-thrombin III levels.

Potential therapeutic strategies focusing on replenishing and maintaining the level of the reduced high-molecular-weight multimer of the vWF factor may offer a therapeutic potential for management of patients with bleeding angiectasias and remain to be explored. Replacement therapies that have been traditionally used for treatment of patients with von Willebrand’s disease (factor VIII/vWF concentrates) are, however, relatively deficient in the high-molecular-weight multimers of vWF; and this may explain their lack of apparent benefit in treating patients with bleeding angiectasias.

**Endoscopic Intervention for Angioectasias**

Endoscopic therapy through a push enteroscope has been shown to improve the outcome in patients with angioectasias. In a retrospective comparative study of 83 patients with GI bleeding from small bowel angiectasias, cautery of the angiectasias decreased bleeding and the need for transfusions compared with controls (0.32 ± 0.91 vs 2.40 ± 3 units/month; P < .001) during a follow-up of 26 months. On average, the treated patients underwent 1.9 sessions of cautery. Another smaller study of 20 patients confirmed these observations; there was a reduced need for transfusions from 13 ± 6 units of packed red cells per year to 6 ± 3 units after cautery (P = .02), and 31% of patients no longer required transfusions. In a study of 11 patients with transfusion-dependent bleeding from angiectasias, a single session of cautery of 2 lesions resulted in significant improvement of the hemoglobin level from 8.5 to 13.5 g/dL (P < .01) during 6 months after therapy. Current evidence supports improved patient outcomes after endoscopic treatment via push enteroscopy, up to an additional 20%–40% benefit over the spontaneous cessation of bleeding.

**Angiographic Therapy**

Angiographic therapy is usually reserved for acutely bleeding lesions detected during diagnostic angiography. The minimal bleeding rate for angiographic detection is approximately 0.5 mL/min. Angiography, however, becomes optimally sensitive when the bleeding rate is at least 1.0 mL/min, which is equivalent to 3 units of blood loss per day. Selective intra-arterial vasopressin therapy had been considered to be the standard therapy, but superselective embolotherapy with microcoils alone or with gelatin sponge pledgets or polyvinyl alcohol embolospheres is becoming increasingly popular. The major advantages of successful embolotherapy are immediate bleeding cessation, which permits angiography catheter removal and avoids the risk of prolonged cath-
In summary, both capsule endoscopy and DBE have revolutionized our approach to the diagnosis and management of patients with obscure GI bleeding. Training in the use of these novel technologies and further research on the optimum utilization of these technologies will improve the quality of care of patients with obscure GI bleeding.

GOTTUMUKKALA S. RAJU
Department of Medicine
University of Texas Medical Branch, Galveston
Galveston, Texas

LAUREN GERSON
Department of Medicine
Stanford University
Stanford, California

ANANYA DAS
Department of Medicine
Mayo Clinic, Scottsdale
Scottsdale, Arizona

BLAIR LEWIS
Department of Medicine
Mount Sinai School of Medicine
New York, New York

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Address requests for reprints to: Chair, Clinical Practice and Economics Committee, AGA Institute National Office, c/o Membership Department, 4930 Del Ray Avenue, Bethesda, Maryland 20814. Fax: (301) 654-5920.

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