Evaluation of suspected small bowel bleeding (formerly obscure gastrointestinal bleeding)

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INTRODUCTION

Bleeding from the small bowel is uncommon, but it is responsible for the majority of patients with gastrointestinal bleeding that persists or recurs without an obvious etiology after upper endoscopy, colonoscopy, and, possibly, radiologic evaluation of the small bowel [1]. In the past, if no source of bleeding was found after an endoscopic evaluation, the bleeding was referred to as being "obscure." However, more recently, it has been proposed that the term obscure only be used if patients have not had a source of bleeding identified after a thorough examination of the entire gastrointestinal tract, including the small bowel [2]. Most cases of what was previously referred to as obscure bleeding are more correctly categorized as suspected small bowel bleeding.

Small bowel bleeding may either be occult or overt:

- Occult bleeding refers to a positive fecal occult blood test result that may or may not be associated with iron deficiency anemia when there is no evidence of visible blood loss to the patient or clinician.
- Overt bleeding refers to bleeding that is visible to the patient or clinician. Overt bleeding may manifest as melena, hematochezia, or rarely in the case of small bowel bleeding, hematemesis.

The evaluation of patients with suspected small bowel bleeding will be reviewed here. The initial evaluation of patients with gastrointestinal bleeding is discussed separately. (See "Evaluation of occult gastrointestinal bleeding" and "Approach to acute upper gastrointestinal bleeding in adults" and "Approach to acute lower gastrointestinal bleeding in adults".)

In 2015, the American College of Gastroenterology published a guideline on the evaluation of small bowel bleeding. The discussion that follows is consistent with that guideline [2]. Similar guidelines have been published in Europe and Japan [3,4].

ETIOLOGY

In patients with gastrointestinal bleeding, approximately 5 to 10 percent will not have a source identified with a standard endoscopic and radiographic evaluation [2,5]. In approximately 75 percent of these patients, the source is in the small bowel [6-9]. The remainder of cases are due to missed lesions in either the upper or lower gastrointestinal tract.

There are multiple potential causes of small bowel bleeding (table 1). Their relative frequencies have not been well defined and, in part, depend on age [10]:

- Patients younger than 40 years are more likely to have inflammatory bowel disease, a Meckel's diverticulum, Dieulafoy lesion, or a small bowel neoplasm (eg, gastrointestinal stromal cell tumor, lymphoma, carcinoid, adenocarcinoma, or polyp).
- Older patients are more likely to have bleeding from vascular lesions, erosions, or ulcers related to nonsteroidal anti-inflammatory drugs. Tumors, both benign and malignant, do occur, but they represent a smaller proportion of the causes of small intestinal bleeding than in patients <40 years of age.

EVALUATION

The evaluation of suspected small bowel bleeding consists of a judicious search for the cause of bleeding, which should be guided by the clinical history, physical findings, and the results of any previous evaluations. Additional tests that may be indicated include wireless video capsule endoscopy, deep small bowel enteroscopy, radiographic imaging (computed tomographic enterography [CTE], computed tomographic angiography [CTA], or magnetic resonance enterography [MRE]), and intraoperative enteroscopy. The most common first step in the evaluation of suspected small bowel bleeding is capsule endoscopy, provided the initial upper

endoscopy and colonoscopy were complete examinations with good visualization (algorithm 1). (See 'Summary and recommendations' below.)

There are several elements from the medical history and physical examination that can provide clues about the cause of bleeding and help define the aggressiveness with which a bleeding site should be sought:

- Recurrent hematemesis indicates bleeding proximal to the ligament of Treitz, usually proximal to the second portion of the duodenum (ie, upper gastrointestinal bleeding rather than small bowel bleeding, which originates distal to the ligament of Treitz), while recurrent passage of bright red blood per rectum suggests a lower gastrointestinal cause. Occasionally, in very hemodynamically unstable patients, bright red blood may originate from the small intestine or duodenum.

- Melena can originate from bleeding anywhere from the nose to the right colon. As a result, the presence of melena has little localization value.

- A history of aortic stenosis should alert the clinician to the possibility of Heyde syndrome. (See "Angiodysplasia of the gastrointestinal tract", section on 'Aortic stenosis'.)

- Gastrointestinal bleeding is common among patients with left ventricular assist devices and is often related to angiodysplasia. (See "Angiodysplasia of the gastrointestinal tract", section on 'Left ventricular assist devices'.)

- A review of over-the-counter medications may reveal use of nonsteroidal anti-inflammatory agents.

- A family history of cancer occurring at an early age, particularly colorectal or endometrial cancer, may suggest the presence of Lynch syndrome. (See "Lynch syndrome (hereditary nonpolyposis colorectal cancer): Clinical manifestations and diagnosis".)

- Skin, nail, and mucosal changes may suggest the presence of several disorders associated with gastrointestinal bleeding or iron deficiency anemia, including:

  - Telangiectasias of the lips or oropharynx (picture 1), which may be due to hereditary hemorrhagic telangiectasia. (See "Clinical manifestations and diagnosis of hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu syndrome)".)

  - Dermatitis herpetiformis, which may be seen with celiac disease. (See "Epidemiology, pathogenesis, and clinical manifestations of celiac disease in adults".)

- Miscellaneous conditions with cutaneous and gastrointestinal manifestations (eg, Kaposi sarcoma, Peutz-Jeghers syndrome, tylosis, pseudoxanthoma elasticum, Ehlers-Danlos syndrome, blue rubber bleb nevus syndrome, immunoglobulin A vasculitis [Henoch-Schönlein purpura], neurofibromatosis, malignant atrophic papulosis, and Klippel-Trénaunay-Weber syndrome). (See appropriate topic reviews).

- Estimation of the rate of blood loss can be based on the change in hematocrit, iron stores, and/or the need for transfusion. A conservative evaluation may be warranted in patients who have serious comorbidities and a slow rate of blood loss.

General approach — The approach to the evaluation of patients with gastrointestinal bleeding and a negative initial evaluation depends on whether the bleeding is occult or overt, if the patient has signs of severe bleeding, and if the patient is healthy enough to undergo an aggressive endoscopic evaluation (algorithm 1).

The evaluation typically starts with repeating an upper endoscopy and/or colonoscopy if the initial examinations were inadequate or if overt bleeding that had stopped recurs. For patients with risk factors for hemobilia or hemosuccus pancreaticus, the upper endoscopy should include evaluation with a side-viewing duodenoscope. Patients with risk factors for an aortoenteric fistula should also undergo CT angiography as part of their initial evaluation. A push enteroscopy should be performed, rather than an upper endoscopy, if a proximal small bowel lesion is suspected. In addition, evaluation for non-gastrointestinal sources of blood loss (eg, lesions in the oropharynx) should be pursued for patients with symptoms or signs suggesting a non-gastrointestinal source, such as nose bleeds, oral lesions, or lymphadenopathy of the head or neck. (See "Overview of the diagnosis and staging of head and neck cancer", section on 'Clinical presentation' and "Approach to the adult with epistaxis", section on 'Evaluation'.)

If the repeat endoscopic evaluation is negative or not needed, the next step is typically wireless video capsule endoscopy. However, for patients with signs of severe bleeding (eg, hypotension, tachycardia, or orthostatic hypotension) a more aggressive evaluation with modalities such as angiography may be indicated (algorithm 2 and algorithm 3). (See "Approach to acute upper gastrointestinal bleeding in adults", section on 'Other diagnostic tests' and "Approach to acute lower gastrointestinal bleeding in adults", section on 'Radiographic imaging'.)

In patients without an obvious source of bleeding on capsule endoscopy, the decision to pursue further testing should consider the rate of blood loss, the presence of comorbidities, and whether there are signs of ongoing bleeding (eg, recurrent overt bleeding or persistent iron deficiency anemia). In patients with significant comorbid illnesses with slow rates of blood loss,

it may be reasonable to stop the evaluation and treat with iron repletion and/or transfusions as needed. Aggressive evaluation with approaches such as deep small bowel enteroscopy is generally warranted in any patient with signs of ongoing bleeding who is in good enough health to warrant it. For patients with a negative evaluation who appear to have stopped bleeding, expectant management is appropriate.

Hemodynamically stable patients — Among patients who are hemodynamically stable without signs of severe bleeding (eg, hypotension, tachycardia, or orthostatic hypotension), the first test obtained is usually video capsule endoscopy, provided there are no contraindications to the study (eg, partial or intermittent small bowel obstruction) (algorithm 1). Because blood loss is typically intermittent both in overt and occult small bowel bleeding, luminal bleeding detected on capsule endoscopy may be followed by a clear lumen on subsequent examination (eg, enteroscopy), to then be followed by more blood or melanotic material. If blood is seen on capsule endoscopy, the origin of the bleeding is likely at or close to the first visualization of blood; bleeding from more than one site is extremely rare.

If the capsule endoscopy is negative and the only manifestation of gastrointestinal bleeding is anemia or occult blood in the stool, patients are managed expectantly with no additional workup, provided the bleeding does not continue or recur. (See 'Wireless video capsule endoscopy' below.)

If the bleeding continues or recurs, if the bleeding was overt, or if the capsule endoscopy results are equivocal, CTE or MRE should be obtained. (See 'Enterography' below.)

If no source is identified and the bleeding continues, the next step is typically deep small bowel enteroscopy. Push enteroscopy with either a dedicated push enteroscope or pediatric colonoscope is an alternative if deep small bowel enteroscopy is not available. If there are contraindications to deep small bowel enteroscopy, intraoperative enteroscopy can be performed. (See 'Deep small bowel enteroscopy' below and "Overview of deep small bowel enteroscopy" and 'Intraoperative enteroscopy' below.)

If deep small bowel enteroscopy is negative and the bleeding continues, additional testing may include a Meckel's scan, angiography, or laparoscopy/laparotomy with intraoperative enteroscopy. We typically perform a Meckel's scan for patients who are under the age of 50 years (though bleeding from a Meckel's diverticulum may occur at any age). In adults the diagnostic yield of a Meckel's scan is lower than in children for unclear reasons. (See 'Radionuclide scanning' below.)

For patients with significant ongoing bleeding (eg, bleeding that requires blood transfusions), we will obtain angiography. While some centers perform a bleeding scan to direct the

angiography, this can lead to failure to visualize the bleeding source on angiography if the bleeding slows or stops during the time it takes to obtain the scan. An alternative is CT angiography; however, it lacks therapeutic capabilities (eg, embolic occlusion of bleeding vessels). We will proceed with intraoperative enteroscopy as a last resort if the patient is a good surgical candidate. (See 'Angiography' below and 'Intraoperative enteroscopy' below.)

Hemodynamically unstable patients — The management of patients who are hemodynamically unstable or have signs of severe bleeding depends on the initial presentation (hematemesis, melena, or hematochezia) (algorithm 2 and algorithm 3). Patients with a left ventricular assist device are often in this category. While capsule endoscopy may help detect the site of bleeding, therapeutic intervention does little to change outcomes [11]. The approaches to these patients are discussed elsewhere. (See "Approach to acute upper gastrointestinal bleeding in adults" and "Approach to acute lower gastrointestinal bleeding in adults".)

DIAGNOSTIC TESTS

Repeat upper endoscopy and colonoscopy — Lesions within reach of a standard upper endoscope or colonoscope may be missed for a variety of reasons; thus, a repeat examination may be warranted. Repeat examinations probably have greatest value in patients with occult bleeding with iron deficiency anemia, or overt bleeding with melena or maroon blood per rectum. Repeat upper endoscopy or colonoscopy should be the first step in the evaluation if either examination was suboptimal when initially performed (eg, if the colonoscopy preparation was poor or the cecum was not reached) (algorithm 1) [12,13].

Lesions that are commonly missed in the upper gastrointestinal tract include Cameron ulcers or erosions in a large hiatus hernia, peptic ulcers on the medial aspect of the junction of the bulb and second part of the duodenum, Dieulafoy lesions, gastric antral vascular ectasia (GAVE), and angioectasia [14-17]. In addition, bleeding stigmata on esophageal or gastric varices may not have been appreciated, particularly in patients who are volume depleted at the time of endoscopy. An aortoenteric fistula should be considered in patients with a history of an abdominal aortic aneurysm repair. Biopsies of the duodenum should be obtained if celiac disease is suspected based upon serologic testing or if iron deficiency anemia is present. Careful inspection of areas that are known to be relatively difficult to visualize should be attempted during repeat upper endoscopy, including the incisura angularis, the superior aspect of the lesser curvature, and fornices of the duodenal bulb. A side-viewing duodenoscope may be of value in examining the medial aspect of the second part of the duodenum and periampullary area. (See "Causes of upper gastrointestinal bleeding in adults", section on 'Specific causes'.)

Some of the lesions that may be missed in the colon include colon cancer, angioectasia, diverticula, and inflammatory bowel disease [18]. While hemorrhoidal bleeding can lead to bleeding and anemia, it is an uncommon that it is identified as the cause of bleeding in patients who have already undergone a colonoscopy [19]. Because hemorrhoidal bleeding is minor in most patients, hemorrhoids may not be recognized as an important source of more serious blood loss. A flexible sigmoidoscopy (without a bowel preparation) on the day of bleeding can help point to hemorrhoids as the cause of bleeding if blood is seen in the rectum but not more proximally. Such patients should be referred to a colorectal surgeon for further evaluation and treatment. Conversely, bleeding leading to iron deficiency anemia should not be attributed to hemorrhoids unless significant bleeding from hemorrhoids is reported by the patient, bleeding is seen during an endoscopic evaluation, and other sources have been excluded. (See "Home and office treatment of symptomatic hemorrhoids".)

The frequency of lesions missed on upper endoscopy or colonoscopy was examined in a study of 317 patients who underwent capsule endoscopy for suspected small bowel bleeding [18]. A bleeding source was found outside of the small bowel in 11 patients (4 percent). The source of the bleeding was found in the upper gastrointestinal tract in four patients, and the lesions included gastric cancer (one patient) and angioectasia of the stomach or duodenum (three patients, including one case of GAVE). In seven patients, the bleeding source was identified in the colon. The lesions found in the colon included colon cancer (three patients), angioectasias (two patients), a diverticulum (one patient with overt bleeding), and colitis from Crohn disease (one patient).

Wireless video capsule endoscopy — Wireless video capsule endoscopy is generally the test of choice for evaluating suspected small bowel bleeding in patients who have had an adequate upper endoscopy and colonoscopy. Its main advantages are that it is noninvasive and it permits examination of the entire length of the small bowel most of the time. Its main disadvantages are that it does not permit tissue sampling or therapeutic intervention, and that not all of the small bowel mucosa is visualized. This section will review the use of capsule endoscopy in patients with suspected small bowel bleeding. A more detailed discussion of capsule endoscopy can be found elsewhere. (See "Wireless video capsule endoscopy".)

Capsule endoscopy is contraindicated in some patients, including those with partial or intermittent small bowel obstruction, women who are pregnant, and patients who are unable to swallow the capsule (though endoscopic placement is an option in many of these patients). In such patients, options include enteroscopy and radiographic imaging. There remains a US Food and Drug Administration boxed warning in the capsule labeling that contraindicates capsule endoscopy in patients with pacemakers and implantable defibrillators. However, studies have

not found evidence that the devices interfere with one another (ie, the capsule does not appear to interfere with the functioning of cardiac devices, and cardiac devices do not appear to interfere with capsule imaging) [20,21]. However, left ventricular assist devices may cause loss of images if the capsule endoscopy sensors are placed too close to the device. (See "Wireless video capsule endoscopy", section on 'Contraindications' and 'Enteroscopy' below and 'Radiographic imaging' below.)

Comparison with other methods — Studies suggest that capsule endoscopy is equally or more sensitive than other methods for the diagnosis of small bowel sources of blood loss [10,22,23]. (See "Wireless video capsule endoscopy", section on 'Suspected small bowel bleeding/iron deficiency anemia'.)

Randomized trials have found the following [10]:

- One trial with 89 patients with suspected small bowel bleeding compared capsule endoscopy with push enteroscopy [22]. It found that performing capsule endoscopy before push enteroscopy was a more effective strategy than beginning with push enteroscopy. After 12 months of follow-up, a strategy based on capsule endoscopy first (followed by push enteroscopy as necessary) had a similar diagnostic yield, clinical outcome, and therapeutic impact compared with a strategy of push enteroscopy first (followed by capsule endoscopy as needed). However, the capsule endoscopy first strategy significantly reduced the percentage of patients needing the alternative study (25 versus 79 percent).

- In a randomized trial with 136 patients with suspected small bowel bleeding who had undergone upper endoscopy, colonoscopy, and push enteroscopy, patients were assigned to either capsule endoscopy or radiographic evaluation [23]. The diagnostic yield was higher for capsule endoscopy (30 versus 7 percent). However, after 12 months of follow-up, there was no difference in the rate of recurrent bleeding between those who underwent capsule endoscopy and those who underwent radiographic evaluation (30 versus 24 percent).

Efficacy — The diagnostic yield of capsule endoscopy in patients with overt bleeding appears to be highest when it is performed as close as possible to the bleeding episode [24-28]. In patients with ongoing overt bleeding, the yield for capsule endoscopy has been reported to be greater than 90 percent. However, if the capsule endoscopy is obtained one to two weeks after the bleeding has stopped, a source is found in only two-thirds of patients. After two weeks, the reported yield drops to less than 10 percent. Among inpatients, the early use of capsule endoscopy (less than three days after admission) has been associated with better outcomes

compared with capsule endoscopy performed three or more days after admission. In a study that included 144 in patients with suspected small bowel bleeding, early capsule endoscopy resulted in a higher detection rate of active bleeding or angioectasia (44 versus 28 percent), more patients receiving therapeutic interventions (19 versus 7 percent), and shorter mean length of stay (6 versus 10 days) [29].

The small intestine acts as a peristaltic pump. Thus, if bleeding is substantial and proximal there may be multiple boluses of blood with normal intervening luminal contents for long distances down the intestine. These may be bright red if the bleeding is substantial, or the blood may be in various degrees of degradation towards hematin if the bleeding is slower. There is very little retrograde flow of blood, thus the likely source of bleeding is very close to the first sign of blood in the lumen. Multiple simultaneous sites of bleeding typically do not occur except in patients with left ventricular assist devices and those with severely supratherapeutic anticoagulation. A small study that interpreted the suspected blood indicator using the Medtronic system showed that if there were more than eight contiguous red bars there was 100 percent likelihood of there being active bleeding [30]. In general, the suspected blood indicator is not very sensitive or specific due to interference by luminal bubbles.

Testing with a fecal immunochemical test (FIT) for occult blood may help with the timing of capsule endoscopy in patients with suspected small bowel bleeding. In one study with 202 patients with suspected small bowel bleeding who had both capsule endoscopy and FIT, a positive FIT was associated with higher likelihood of ulcers, tumors, and active bleeding [31]. In patients with occult bleeding who had capsule endoscopy on the same day or the day after FIT, the prevalence of small bowel disease was significantly higher in the positive than negative FIT group (54 versus 13 percent; $p = 0.001$), while there was no significant difference between positive and negative FIT groups who had capsule endoscopy two days or more after FIT. This suggests that in patients with suspected small bowel bleeding and a positive FIT, capsule endoscopy should be performed within a day if possible. However, this report is open to question since FIT testing is designed to detect colonic bleeding and not small intestinal bleeding. The older guaiac-based test does not discriminate in terms of the origin of bleeding, and while less sensitive and specific, may be more appropriate.

However, whether detecting lesions on capsule endoscopy results in lower rebleeding rates is not clear. In a study of 305 patients who underwent capsule endoscopy for suspected small bowel bleeding, significant findings on capsule endoscopy were reported in 157 patients (52 percent) [32]. Treatment was performed in 36 patients (12 percent). Overall, rebleeding occurred in 19 percent of patients. Rebleeding rates did not differ between those with positive and negative capsule endoscopy examinations, or between those who underwent treatment and

those who did not. Factors that were associated with an increased risk of rebleeding included the presence of angioectasia (hazard ratio [HR] 1.82, 95% CI 1.04-3.20) and a >3 month duration of gastrointestinal bleeding (HR 1.64, 95% CI 1.10-2.46).

Repeat capsule endoscopy — Repeat capsule endoscopy has been proposed for patients whose initial capsule endoscopy is negative. In a retrospective study of 676 patients, 82 (12 percent) had repeat capsule studies. Overall, the diagnostic yield was 55 percent and successful management was achieved in 39 percent [33]. The yield was highest in patients with a prior positive study (77 percent) and was lowest in patients with ongoing symptoms and a prior negative study (32 percent). The high yields for repeat capsule endoscopy in this study may have occurred because capsule endoscopy does not visualize the entire small bowel mucosa on a single pass. This happens because the capsule does not pursue an axial path; rather, it is known to tumble quite frequently [34] and is unable to see behind folds of the small intestine. Our approach is to repeat the capsule endoscopy if the initial examination is suboptimal (eg, if there is impaired visualization due to debris). Further, because intestinal bleeding is usually intermittent, we are increasingly using repeat capsule endoscopy in patients with overt or transfusion-requiring occult bleeding to localize the source of bleeding as a guide to therapeutic intervention.

Enteroscopy — Enteroscopy involves the passage of an adult or pediatric colonoscope or a dedicated enteroscope beyond the ligament of Treitz. Several methods of enteroscopy have been described such as push, intraoperative, and deep small bowel enteroscopy (including single balloon, double balloon, and spiral enteroscopy). These methods differ in their ability to reach the distal small bowel and permit therapeutic interventions. In patients with a negative capsule endoscopy and computed tomographic (CT) enterography with ongoing bleeding, the next step in the evaluation is typically deep small bowel enteroscopy, if available. Push enteroscopy, which is able to evaluate the proximal small bowel, is an alternative if deep small bowel enteroscopy is not available or for patients at risk of having an aortoenteric fistula (eg, those with a prior aortic aneurysm repair), though in such patients, CT angiography is usually the initial test obtained. Intraoperative enteroscopy is an option if deep small bowel or push enteroscopy does not reveal a bleeding source, if there is massive bleeding with hemodynamic instability, or if there are contraindications to deep small bowel enteroscopy, such as dense abdominal adhesions. (See "Causes of upper gastrointestinal bleeding in adults", section on 'Aortoenteric fistulas'.)

Push enteroscopy — Push enteroscopy involves per oral passage of a dedicated push enteroscope or a colonoscope past the ligament of Treitz. The instruments are 200 to 250 cm long, though the depth of insertion is often limited by looping and patient discomfort.

Depending on the equipment and techniques used, it is estimated that 25 to 80 cm of jejunum distal to the ligament of Treitz can be evaluated [35].The amount of jejunum examined is enhanced when an overtube designed to reduce looping in the stomach is used; whether this improves its diagnostic and therapeutic ability is unsettled [36,37].

Multiple studies have described the diagnostic yield of push enteroscopy in identifying bleeding lesions with estimates ranging from 3 to 70 percent [10]. Angioectasia is the most common diagnosis (as high as 80 percent in one report) [14,38,39]. An advantage of push enteroscopy compared with capsule endoscopy is the ability to sample tissue and to perform therapeutic maneuvers.

An illustrative study included 95 patients with suspected small bowel bleeding who underwent push enteroscopy. A suspected source of bleeding was detected in 39 patients (41 percent), 16 of whom underwent endoscopic treatment [14]. An important observation from this study was that many of the lesions detected during enteroscopy were within reach of a standard endoscope, indicating that a careful repeat standard upper endoscopy may be appropriate prior to push enteroscopy or other diagnostic studies. (See 'Repeat upper endoscopy and colonoscopy' above.)

Deep small bowel enteroscopy — Methods for deep small bowel enteroscopy include double balloon enteroscopy, single balloon enteroscopy, and spiral enteroscopy. All of the deep enteroscopy techniques allow for both evaluation and therapeutic intervention in the small bowel. The techniques are based on different designs of overtube, which fit over a flexible, thin enteroscope. Each is designed to minimize looping of the small bowel while pleating it back over the enteroscope and overtube, analogous to a shower curtain on a rod. The balloon devices can be used anterograde or retrograde. The spiral overtube has been widely used via the anterograde route, but little has been reported on its use in a retrograde direction. The use of a combination of anterograde and retrograde enteroscopy may allow complete enteroscopy. (See "Overview of deep small bowel enteroscopy".)

Most of the data available on the efficacy of deep small bowel enteroscopy for the evaluation of suspected small bowel bleeding are from studies of double balloon enteroscopy. In a retrospective study from Japan, double balloon enteroscopy detected bleeding sources in 155 of 200 patients (78 percent) with suspected small bowel bleeding [40]. Small intestinal ulcers and erosions were the most common findings (64 patients). The yield was higher in the patients who underwent double-balloon enteroscopy within one month of an episode of overt bleeding compared with patients who did not (84 versus 57 percent). The overall rate of bleeding control was 64 percent. In patients with small intestinal vascular lesions, rebleeding was more common

in patients who had large transfusion requirements before double balloon enteroscopy, multiple lesions, or suspicious (as opposed to definite) bleeding sources identified.

A cost-effectiveness analysis comparing double balloon enteroscopy with capsule endoscopy for patients with overt bleeding found that an initial double balloon enteroscopy was cost-effective, but that capsule-directed double balloon enteroscopy may be associated with better long-term outcomes because of fewer complications and decreased utilization of endoscopic resources [41,42].

Intraoperative enteroscopy — Intraoperative enteroscopy involves the insertion of an endoscope through an enterotomy site, orally, or rectally during surgery [43,44]. The approach via an enterotomy has become difficult in the United States because of the withdrawal of ethylene oxide gas sterilization of endoscopic equipment. No substitute is currently available. The surgeon telescopes the bowel over the endoscope, allowing inspection of the entire length of small bowel in more than 90 percent of patients. The diagnostic yield has been reported to be in the range of 60 to 88 percent, with rates of recurrent bleeding of 13 to 60 percent [10]. In general, intraoperative enteroscopy is avoided unless there is no known target established by endoscopy or imaging. However, it may be the only option in patients with significant ongoing bleeding who do not have a bleeding source identified by less invasive means. If deep enteroscopy (antegrade or retrograde) is performed prior to intraoperative enteroscopy and a tattoo is placed at the site of maximum insertion, it limits the need for total intestinal examination at intra-operative enteroscopy if a small tumor is suspected.

Intraoperative enteroscopy has been associated with complications and deaths. In one report, for example, morbidity included serosal tears (two requiring resection), avulsion of the superior mesenteric vein, congestive heart failure, azotemia, and prolonged ileus [44]. However, a more recent prospective study demonstrated an excellent correlation between capsule endoscopy and intraoperative enteroscopy with fewer complications [24].

A large, multidisciplinary study employing intra-operative enteroscopy for patients who had bleeding or anemia had a diagnostic yield of 69 percent. Segmental resection was performed in 90 percent of these patients, with a symptom recurrence rate of 20 percent. No serious complications were reported [45]. It should be understood that the safe insertion of an enteroscope via an enterotomy is limited by the radius of curvature of the scope and the length of the mesentery. It is much safer, if complete examination of the small intestine is needed, to do one or more enterotomies than to overstretch and tear the mesentery and its vessels.

Radiographic imaging — Radiographic studies that are available for the evaluation of suspected small bowel bleeding include enterography, radionuclide scanning, and angiography.

For the most part, radiographic studies have been replaced by wireless video capsule endoscopy and deep small bowel enteroscopy. Exceptions are CT enterography and angiography, which still have a role in the evaluation. Small bowel series using barium should not be performed for the evaluation of suspected small bowel bleeding [2].

Enterography — CT enterography and magnetic resonance enterography are studies in which low-density oral contrast is used to distend the small bowel, allowing for better visualization of the small bowel wall. A multiphasic CT enterography using an occult gastrointestinal or suspected small bowel bleeding protocol (with an arterial phase, enteric phase, and delayed phase) is used to detect vascular, mucosal, and mass lesions. (See "Diagnosis and staging of small bowel neoplasms".)

In a meta-analysis of 18 studies, the yield of CT enterography for detecting a source of suspected small bowel bleeding was 40 percent (95% CI 33-49 percent) [46]. The yield appears to be highest in patients with a history of massive bleeding [47].

Radionuclide scanning — Radionuclide imaging includes bleeding scans and scans to detect a Meckel's diverticulum. A radionuclide bleeding scan detects bleeding that is occurring at a minimum rate of 0.1 to 0.5 mL/minute. It is of little or no value in patients with gastrointestinal bleeding who appear clinically to have a low rate of blood loss (such as those with occult blood only) since the rate of bleeding is likely to be too slow to be detected. Bleeding scans may be more sensitive than angiography but less specific than either a positive endoscopic or angiographic examination. A bleeding scan is often requested by interventional radiologists as a prelude to angiography to confirm active bleeding. If a scan is negative, it is unlikely that angiography, a procedure with significant complications, will be positive. However, performing a bleeding scan prior to angiography can lead to failure to visualize the bleeding source on angiography if the bleeding slows or stops during the time it takes to obtain the scan. (See "Angiographic control of nonvariceal gastrointestinal bleeding in adults", section on 'Lesion localization'.)

Two types of nuclear bleeding scans have been used: technetium (99mTc) sulfur colloid and 99mTc pertechnetate-labeled autologous red blood cells. Advantages common to both techniques are noninvasiveness and high sensitivity. A major disadvantage of both imaging techniques is that they only localize bleeding to an area of the abdomen, with accuracy rates ranging from 24 to 91 percent. In addition, the study is purely diagnostic, so if a bleeding source is identified, additional interventions (such as angiography) are typically required. (See "Approach to acute lower gastrointestinal bleeding in adults", section on 'Radionuclide imaging'.)

A Meckel's scan consists of the intravenous administration of 99mTc pertechnetate, which has an affinity for gastric mucosa, followed by scintigraphy to identify areas of ectopic gastric mucosa. The test does not detect active bleeding. Theoretically, the scan should identify only those diverticula that contain ectopic gastric mucosa. While a Meckel's diverticulum can result in bleeding in patients of all ages, most are young. If other tests are unrevealing, a Meckel's scan may reveal a potential bleeding source and is particularly appropriate in children and young adults. The test is less sensitive in adults than it is in children (63 versus 85 percent) [48]. (See "Meckel's diverticulum".)

Angiography — Angiography is usually not helpful in the evaluation of patients with suspected small bowel bleeding unless there are signs of significant active bleeding. We typically use angiography for patients with overt bleeding severe enough to require a transfusion, patients who have (or recently had) signs of hemodynamic instability, or patients who have a positive bleeding scan. It may also be used for the detection of ectopic varices in patients who have bled and who have portal hypertension, but do not have varices in the esophagus or stomach. An advantage with angiography is that embolization can be performed when vascular lesions are discovered. However, embolization of a bleeding site in the small intestine has a significant risk of causing infarction of the intestine. (See "Angiographic control of nonvariceal gastrointestinal bleeding in adults".)

One study that compared capsule endoscopy with angiography in patients with overt bleeding suspected to be originating in the small bowel found that the yield of immediate capsule endoscopy was higher than angiography (53 versus 20 percent), and the risk of rebleeding was lower (17 versus 33 percent) [49]. However, there was no difference between the groups with regard to long-term outcomes such as need for further transfusions, hospitalization for rebleeding, or mortality.

An alternative to percutaneous angiography is CT angiography. However, it does not provide therapeutic capability if a bleeding source is identified. (See "Approach to acute lower gastrointestinal bleeding in adults", section on 'CT angiography'.)

SOCIETY GUIDELINE LINKS

Links to society and government-sponsored guidelines from selected countries and regions around the world are provided separately. (See "Society guideline links: Gastrointestinal bleeding in adults".)

INFORMATION FOR PATIENTS

UpToDate offers two types of patient education materials, "The Basics" and "Beyond the Basics." The Basics patient education pieces are written in plain language, at the 5th to 6th grade reading level, and they answer the four or five key questions a patient might have about a given condition. These articles are best for patients who want a general overview and who prefer short, easy-to-read materials. Beyond the Basics patient education pieces are longer, more sophisticated, and more detailed. These articles are written at the 10th to 12th grade reading level and are best for patients who want in-depth information and are comfortable with some medical jargon.

Here are the patient education articles that are relevant to this topic. We encourage you to print or e-mail these topics to your patients. (You can also locate patient education articles on a variety of subjects by searching on "patient info" and the keyword(s) of interest.)

- Basics topic (see "Patient education: Angiodysplasia of the GI tract (The Basics)")

SUMMARY AND RECOMMENDATIONS

- **Definitions** – Small bowel bleeding may either be occult or overt (see 'Introduction' above):
  - Occult bleeding refers to a positive fecal occult blood test result that may or may not be associated with iron deficiency anemia when there is no evidence of visible blood loss to the patient or clinician.
  - Overt bleeding refers to bleeding that is visible to the patient or clinician. Overt bleeding may manifest as melena, hematochezia, or rarely in the case of small bowel bleeding, hematemesis.
- **Evaluation** – The approach to the evaluation of patients with gastrointestinal bleeding and a negative initial evaluation depends on whether the bleeding is occult or overt, if the patient has signs of severe bleeding, and if the patient is healthy enough to undergo an aggressive endoscopic evaluation (algorithm 1). (See 'General approach' above.)
  - The evaluation typically starts with repeating an upper endoscopy and/or colonoscopy if the initial examinations were inadequate or if overt bleeding that had stopped recurs. For patients with risk factors for hemobilia or hemosuccus pancreaticus, the upper endoscopy should include evaluation with a side-viewing duodenoscope. Patients with

risk factors for an aortoenteric fistula should also undergo computed tomographic angiography. (See 'Repeat upper endoscopy and colonoscopy' above.)

- A push enteroscopy should be performed, rather than an upper endoscopy, if a proximal small bowel lesion is suspected. (See 'Push enteroscopy' above.)
- For patients who are hemodynamically stable without signs of severe bleeding (eg, hypotension, tachycardia, or orthostatic hypotension), the next step is typically wireless video capsule endoscopy. (See 'Wireless video capsule endoscopy' above.)
- For patients who are hemodynamically unstable or who have signs of severe bleeding, a more aggressive evaluation with modalities such as angiography may be indicated (algorithm 2 and algorithm 3). (See "Approach to acute upper gastrointestinal bleeding in adults", section on 'Other diagnostic tests' and "Approach to acute lower gastrointestinal bleeding in adults", section on 'Radiographic imaging'.)
- In patients without an obvious source of bleeding on capsule endoscopy, the decision to pursue further testing should consider the rate of blood loss, the presence of comorbidities, and whether there are signs of ongoing bleeding (eg, recurrent overt bleeding or persistent iron deficiency anemia). In patients with significant comorbid illnesses with slow rates of blood loss, it may be reasonable to stop the evaluation and treat with iron repletion and/or transfusions as needed. Aggressive evaluation with approaches such as deep small bowel enteroscopy is generally warranted in any patient with signs of ongoing bleeding who is in good enough health to warrant it. For patients with a negative evaluation who appear to have stopped bleeding, expectant management is appropriate. (See 'Hemodynamically stable patients' above.)

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Topic 2625 Version 33.0

GRAPHICS

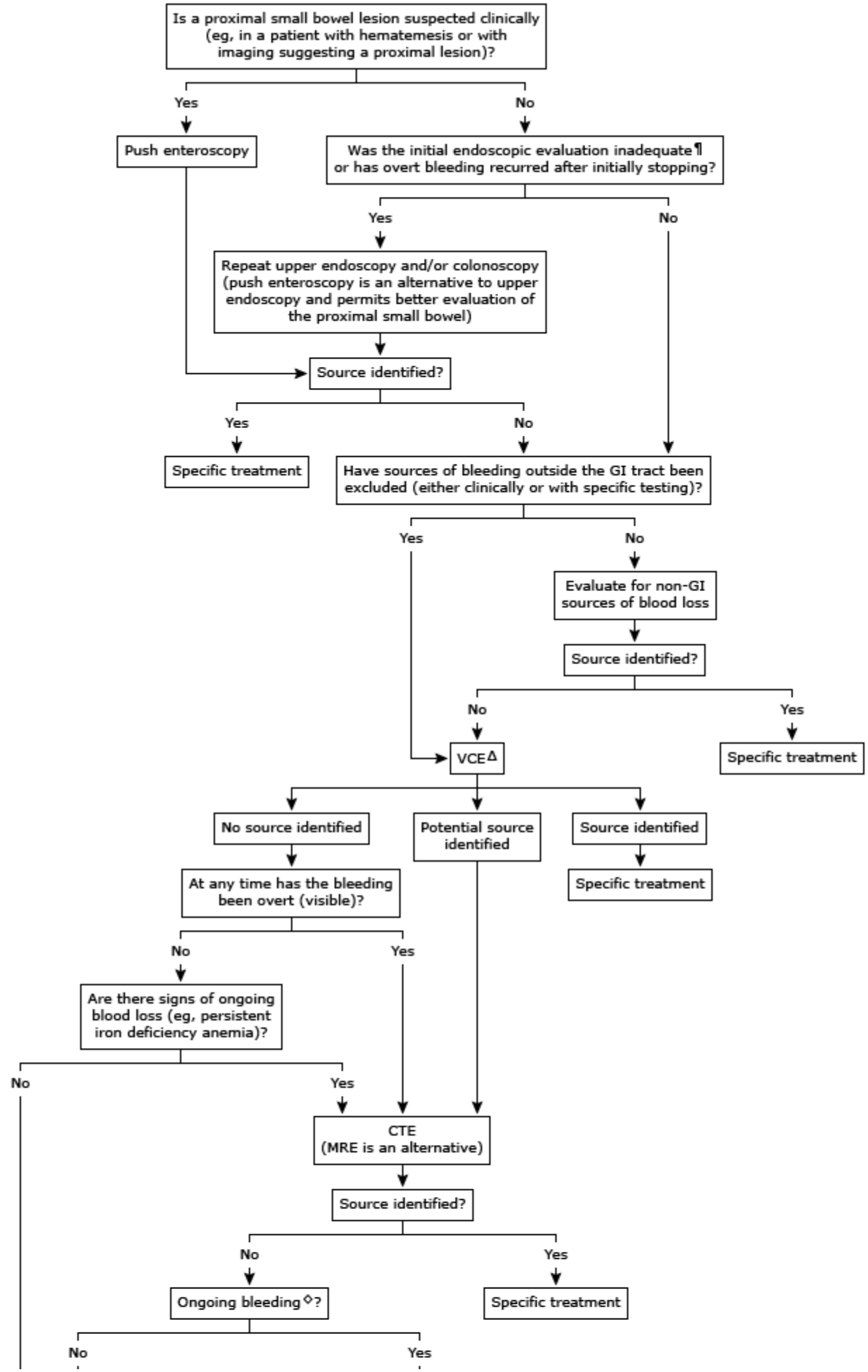
Causes of small bowel bleeding

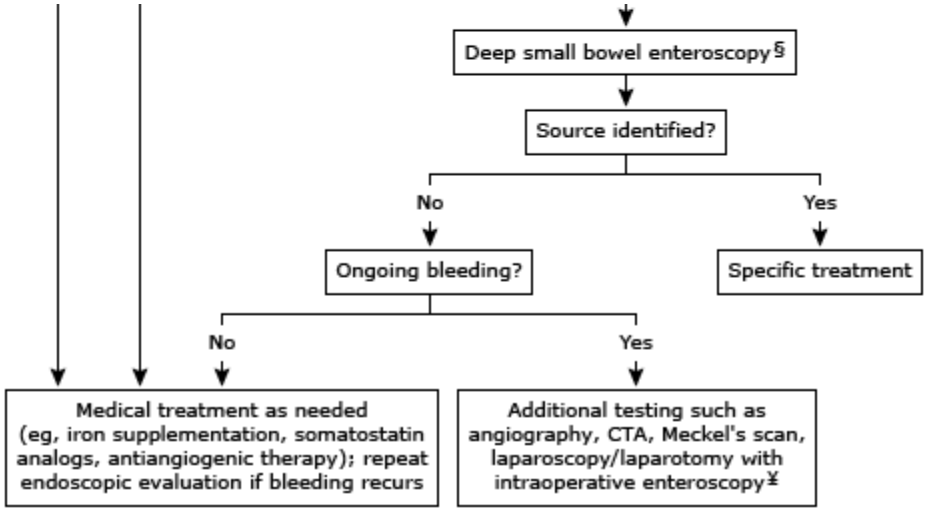
Common causes		Rare causes
Under age 40 years	**Over age 40 years**	
▪ Inflammatory bowel disease ▪ Meckel's diverticulum ▪ Dieulafoy lesions ▪ Neoplasia ▪ Polyposis syndromes	▪ NSAID ulcers ▪ Angioectasia ▪ Dieulafoy lesions ▪ Neoplasia	▪ Immunoglobulin A vasculitis (Henoch-Schöenlein purpura) ▪ Small bowel varices and/or portal hypertensive enteropathy ▪ Amyloidosis ▪ Blue rubber bleb nevus syndrome ▪ Pseudoxanthoma elasticum ▪ Hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu syndrome) ▪ Kaposi sarcoma with AIDS ▪ Plummer-Vinson syndrome ▪ Ehlers-Danlos syndrome ▪ Inherited polyposis syndromes (FAP, Peutz-Jeghers) ▪ Malignant atrophic papulosis ▪ Hematobilia ▪ Aortoenteric fistula ▪ Hemosuccus entericus

FAP: familial adenomatous polyposis; NSAID: nonsteroidal anti-inflammatory drug.

Graphic 104990 Version 3.0

Evaluation of suspected small bowel bleeding in hemodynamically stable patients*


Is a proximal small bowel lesion suspected clinically (eg, in a patient with hematemesis or with imaging suggesting a proximal lesion)?
Yes
No
Push enteroscopy
Was the initial endoscopic evaluation inadequate¶ or has overt bleeding recurred after initially stopping?
Yes
No
Repeat upper endoscopy and/or colonoscopy (push enteroscopy is an alternative to upper endoscopy and permits better evaluation of the proximal small bowel)
Source identified?
Yes
No
Specific treatment
Have sources of bleeding outside the GI tract been excluded (either clinically or with specific testing)?
Yes
No
Evaluate for non-GI sources of blood loss
Source identified?
No
Yes
Specific treatment
VCE△
No source identified
Potential source identified
Source identified
Specific treatment
At any time has the bleeding been overt (visible)?
No
Yes
Are there signs of ongoing blood loss (eg, persistent iron deficiency anemia)?
No
Yes
CTE (MRE is an alternative)
Source identified?
No
Yes
Specific treatment
Ongoing bleeding◇?
No
Yes



GI: gastrointestinal; VCE: video capsule endoscopy; CTE: computed tomographic enterography; MRE: magnetic resonance enterography; CTA: computed tomographic angiography.

* Small bowel bleeding should be suspected in patients with signs of GI bleeding who have had a negative initial endoscopic evaluation (typically upper endoscopy and colonoscopy). The evaluation of hemodynamically unstable patients is discussed in the context of the specific bleeding manifestations (eg, hematemesis). Refer to UpToDate topic reviews on the evaluation and management of GI bleeding for details.

¶ For patients with risk factors for hemobilia or hemosuccus pancreaticus, the upper endoscopy should have included evaluation with a side-viewing duodenoscope. Patients with risk factors for an aortoenteric fistula should also have undergone CTA. If the initial upper endoscopy and/or colonoscopy was inadequate (eg, fair or poor visualization, failure to reach the cecum), repeat examination should be considered before initiating an evaluation for small bowel bleeding.

Δ VCE should be done as close to the acute bleeding episode as possible to increase diagnostic yield. Patients at risk for capsule retention should undergo small bowel imaging (eg, CTE) or a patency capsule study prior to VCE.

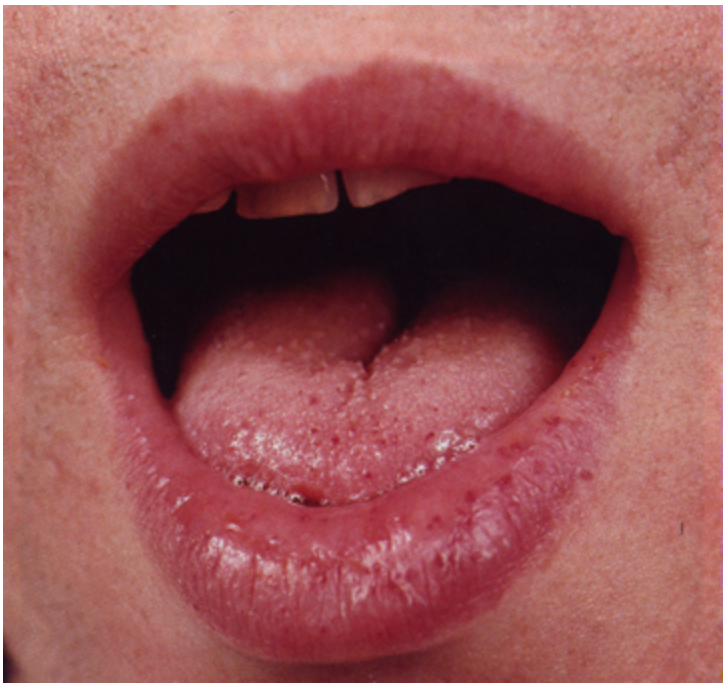
◇ In patients with significant comorbid illnesses with slow rates of blood loss, it may be reasonable to stop the evaluation and treat with iron repletion and/or transfusions as needed.

§ Push enteroscopy is an alternative if not already done and if deep small bowel enteroscopy is not available. Intraoperative enteroscopy is an alternative if there are contraindications to deep small bowel enteroscopy, such as dense intra-abdominal adhesions.

¥ The choice of test will depend on the rate of bleeding, patient characteristics, and the degree of suspicion for a small bowel lesion. A Meckel's scan should be performed in younger patients with overt bleeding. Angiography or CTA can be obtained if there is active bleeding. Surgical exploration is appropriate if no other studies have revealed a source and significant bleeding continues or if there is high suspicion for a small bowel neoplasm. If the evaluation is still negative, non-GI sources of blood loss should be reconsidered.

Graphic 95608 Version 4.0

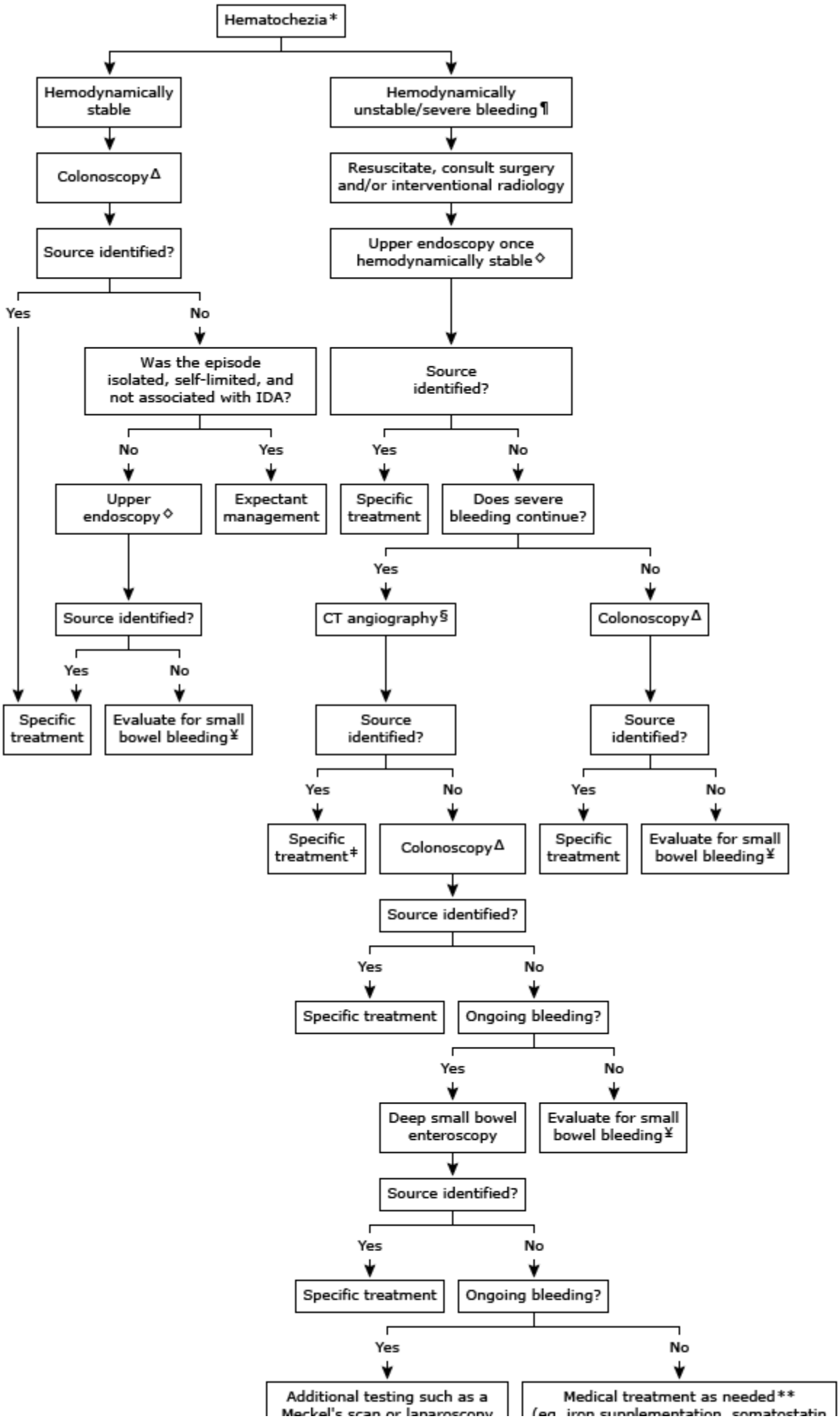
Oral telangiectasia in hereditary hemorrhagic telangiectasia (Osler-Weber-Rendu syndrome)

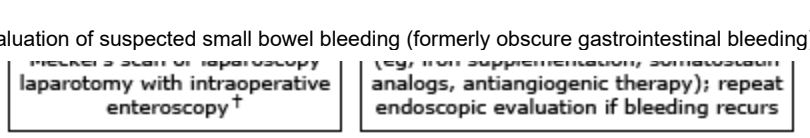


Osler-Weber-Rendu syndrome (also known as hereditary hemorrhagic telangiectasia). Note the multiple 1 to 2 mm, discrete, red macular and papular telangiectases on the lower lip and tongue.

Graphic 52483 Version 6.0

Evaluation of patients presenting with hematochezia (excluding those with minimal rectal bleeding)


Hematochezia*
Hemodynamically stable
Hemodynamically unstable/severe bleeding¶
Colonoscopy△
Resuscitate, consult surgery and/or interventional radiology
Source identified?
Upper endoscopy once hemodynamically stable◇
Yes
No
Was the episode isolated, self-limited, and not associated with IDA?
Source identified?
No
Yes
Yes
No
Upper endoscopy◇
Expectant management
Specific treatment
Does severe bleeding continue?
Yes
No
Source identified?
CT angiography§
Colonoscopy△
Yes
No
Specific treatment
Evaluate for small bowel bleeding¥
Source identified?
Source identified?
Yes
No
Yes
No
Specific treatment‡
Colonoscopy△
Specific treatment
Evaluate for small bowel bleeding¥
Source identified?
Yes
No
Specific treatment
Ongoing bleeding?
Yes
No
Deep small bowel enteroscopy
Evaluate for small bowel bleeding¥
Source identified?
Yes
No
Specific treatment
Ongoing bleeding?
Yes
No
Additional testing such as a
Medical treatment as needed**



IDA: iron deficiency anemia; CTA: computed tomographic angiography; CT: computed tomographic; GI: gastrointestinal; MR: magnetic resonance.

* If hematemesis or melena is present the patient should be evaluated for upper GI bleeding. Refer to UpToDate topics on the evaluation of upper GI bleeding for details.

¶ Bleeding associated with signs such as hypotension, tachycardia, or orthostatic hypotension.

Δ Colonoscopy should be performed once the patient has been resuscitated and an adequate bowel preparation has been given (typically 4 to 6 L of polyethylene glycol). If the initial colonoscopy was inadequate (eg, inadequate visualization, failure to reach the cecum), repeat colonoscopy should be considered.

◇ Consider evaluation with a side-viewing duodenoscope in patients with risk factors for hemobilia or hemosuccus pancreaticus or CT angiography (followed by push enteroscopy if the CT angiography is negative) in patients at risk for an aortoenteric fistula. Conventional transvenous angiography is typically performed if the patient remains hemodynamically unstable despite attempts at resuscitation. If the suspicion for an upper GI source is moderate (rather than high), nasogastric lavage can be performed to look for evidence to support an upper GI source. Refer to UpToDate topics on lower GI bleeding in adults for additional details.

§ Positive CT angiography should be promptly referred for transcatheter angiography and embolization.

¥ Refer to UpToDate topic review on suspected small bowel bleeding for details.

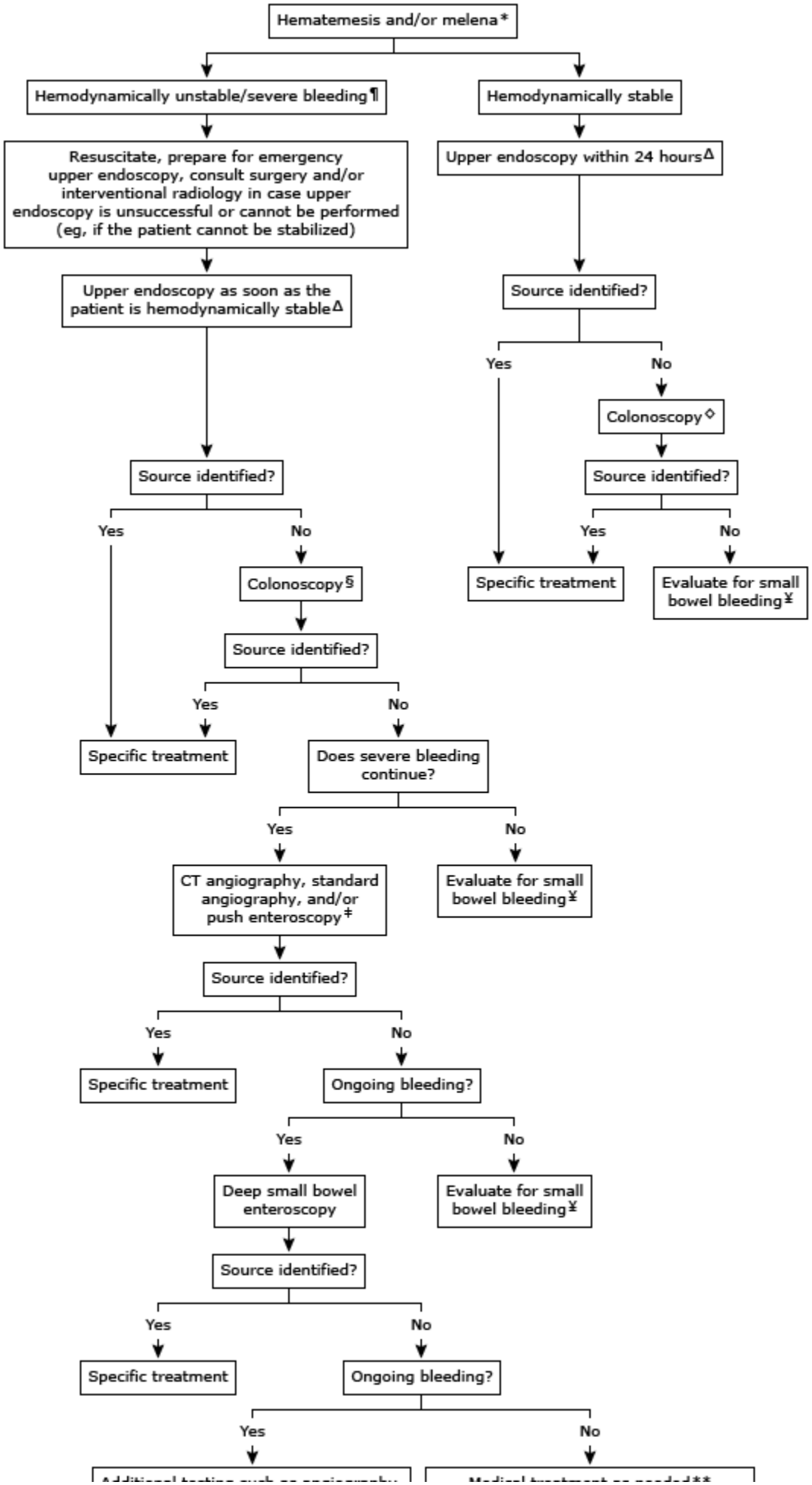
‡ Following successful angiography, an elective colonoscopy may still need to be performed to evaluate the underlying cause of bleeding (eg, large colorectal polyp or neoplasia).

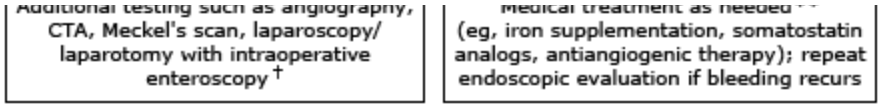
† A Meckel's scan should be performed in younger patients with overt bleeding. Surgical exploration is appropriate if no other studies have revealed a source and significant bleeding continues or if there is high suspicion for a small bowel neoplasm.

** If the deep small bowel enteroscopy was incomplete, a video capsule endoscopy study should be obtained, followed by CT or MR enterography if the capsule endoscopy is negative.

Graphic 95345 Version 8.0

Evaluation of suspected upper gastrointestinal bleeding


Hematemesis and/or melena*
Hemodynamically unstable/severe bleeding¶
Hemodynamically stable
Resuscitate, prepare for emergency upper endoscopy, consult surgery and/or interventional radiology in case upper endoscopy is unsuccessful or cannot be performed (eg, if the patient cannot be stabilized)
Upper endoscopy within 24 hours△
Upper endoscopy as soon as the patient is hemodynamically stable△
Source identified?
Yes
No
Colonoscopy◇
Source identified?
Yes
No
Specific treatment
Evaluate for small bowel bleeding¥
Source identified?
Yes
No
Colonoscopy§
Source identified?
Yes
No
Specific treatment
Does severe bleeding continue?
Yes
No
CT angiography, standard angiography, and/or push enteroscopy‡
Evaluate for small bowel bleeding¥
Source identified?
Yes
No
Specific treatment
Ongoing bleeding?
Yes
No
Deep small bowel enteroscopy
Evaluate for small bowel bleeding¥
Source identified?
Yes
No
Specific treatment
Ongoing bleeding?
Yes
No



GI: gastrointestinal; CT: computed tomographic; CTA: computed tomographic angiography; MR: magnetic resonance.

* The presence of both hematemesis and melena suggests that brisk bleeding is present.

¶ Bleeding associated with signs such as hypotension, tachycardia, or orthostatic hypotension.

Δ Consider evaluation with a side-viewing duodenoscope if there are risk factors for hemobilia or hemosuccus pancreaticus; consider CTA (followed by push enteroscopy if the CTA is negative) in patients at risk for an aortoenteric fistula. Conventional angiography is typically performed if the patient remains hemodynamically unstable despite attempts at resuscitation.

◇ Patients who present with hematemesis do not need to undergo colonoscopy, since hematemesis suggests the bleeding is proximal to the ligament of Treitz. They should proceed directly to an evaluation for small bowel bleeding if upper endoscopy is negative. Colonoscopy is the next step in the evaluation of patients with melena.

§ If the patient becomes hemodynamically unstable following initial resuscitation, conventional angiography can be performed. Patients who present with hematemesis do not need to undergo colonoscopy and can skip this step in the evaluation because hematemesis suggests the bleeding is proximal to the ligament of Treitz.

¥ If the initial endoscopic evaluation was inadequate (eg, fair or poor visualization, failure to reach the cecum), repeat examination should be considered before initiating an evaluation for small bowel bleeding. Refer to UpToDate topic review on suspected small bowel bleeding for details.

‡ If not already done. If the patient remains hemodynamically stable and does not have evidence of aggressive bleeding (eg, ongoing hematochezia), perform a CTA or push enteroscopy (CTA is the initial test of choice if there is concern for an aortoenteric fistula). If the patient becomes hemodynamically unstable following initial resuscitation or has signs of aggressive bleeding, perform conventional angiography.

† If not already done, angiography or CTA may be obtained. If angiography or CTA has been performed and no source is identified, a Meckel's scan should be obtained in younger patients with overt bleeding, unless the only manifestation of bleeding was hematemesis. Surgical exploration is appropriate if no other studies have revealed a source and significant bleeding continues or if there is high suspicion for a small bowel neoplasm.

** If the deep small bowel enteroscopy was incomplete, a video capsule endoscopy study should be obtained, followed by CT enterography or MR enterography if the

capsule endoscopy is negative.

Graphic 105093 Version 4.0

Contributor Disclosures

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