Chapter 1
An Introduction to the Clinical Approach and Management of Occult Gastrointestinal Bleeding

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Introduction and Definitions

The clinical presentation GI blood loss depends on the location of the bleeding as well as the volume and rate of the bleeding. Minuscule blood loss of 0.5–1.5 mL per day in the GI tract is normal and not visualized, whereas larger blood volumes of 100–200 mL or greater produce visible blood in the stool [3]. Visible bleeding is defined as overt GI bleeding which most commonly presents in one of the following ways: (1) hematemesis – coffee-ground colored emesis typically from an upper GI source, (2) hematochezia – bright red blood or clots typically from a location in the distal GI tract or less commonly a briskly bleeding upper GI source, or (3) melena – tarry, black or maroon colored stool typically from an upper GI source or from degradation of blood in slow transit from the proximal colon [4]. *Occult* GI bleeding is not visible to the naked eye and is defined by a positive fecal occult blood test (FOBT) with or without iron deficiency anemia (IDA) [2]. When enough blood is lost over time and not adequately replaced by the body, iron deficiency can develop and eventually manifests as IDA. Chronic GI blood loss as little as 5–10 ml/day can lead to IDA [5].

In most instances, the cause of overt or occult bleeding is readily identified by esophagogastroduodenoscopy (EGD) and/or colonoscopy. However, when EGD

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M. Tadros, G. Y. Wu (eds.), *Management of Occult GI Bleeding*, Clinical Gastroenterology, https://doi.org/10.1007/978-3-030-71468-0_1

Table 1.1 Definitions of gastrointestinal bleeding

Gastrointestinal bleeding	Typical manifestation	Definition
Overt[a]: Bleeding is visible	Hematemesis	Vomiting of bright red blood or dark colored "coffee-grounds"
	Melena	Black, tarry, foul smelling stool
	Hematochezia	Bright red or maroon, bloody stool
Occult: Bleeding is invisible	Iron deficiency anemia (IDA) and/or	Hemoglobin <13 g/dL in men and < 12 g/dL in women. Often with low mean corpuscular volume MCV < 90 (early IDA may present with a normal MCV).
	Positive fecal occult blood test (FOBT)	Absence of overt bleeding with presence of blood in stool by guaiac or immunohistochemical testing
Obscure: Bleeding is visible or invisible		Recurrent or persistent bleeding that is overt or occult as above but with no source found after comprehensive testing of the upper, mid, and lower GI tract[b]

[a] Patients with overt bleeding may have iron deficiency anemia and will have a positive FOBT
[b]Raju et al. [31]

and colonoscopy fail to identify the source of the bleeding, the term *potential small bowel bleeding* is used. Anatomically, small bowel bleeding includes sources distal to the ampulla of Vater and proximal to the ileocecal valve, much of which is beyond the reach of a traditional enteroscope or colonoscope. If additional testing of the small bowel by video capsule endoscopy (VCE), enteroscopy, or radiographic studies such as angiography are also unable to find the source, the bleeding is termed *obscure*. Of note, prior to technological advancements over the last several decades, the term *obscure* bleeding was used to describe occult or overt bleeding following a normal EGD and colonoscopy and essentially became synonymous with small bowel bleeding. However, with the ability to visualize the small bowel with VCE, since 2001, and deep enteroscopy, since 2004, a small bowel source of GI bleeding is found in >70% of cases that were previously classified as obscure bleeding [2, 6]. Table 1.1 clarifies the often misused definitions.

Findings in Occult GI Bleeding

Iron Deficiency Anemia

Iron is essential for hemoglobin production. Thus the inadequate uptake and storage or excessive loss of iron will eventually lead to anemia, defined as a hemoglobin <13 g/dL in men and < 12 g/dL in women. While iron deficiency anemia (IDA) is most often caused by blood loss, other causes such as hemolysis, malabsorption, or increased demand for iron (such as in neonates and pregnant women) need to be

excluded. IDA is most common in neonates and young children, followed by menstruating and pregnant women, and is least common in male adults. Consequently, when iron deficiency anemia is seen in groups other than premenopausal women, it is often assumed to be due to gastrointestinal loss [5].

Occult GI bleeding typically causes a slow and indolent drop in the hemoglobin along with other lab markers of iron deficiency including low serum iron, high iron-binding capacity, and low serum ferritin levels in early stages. Microcytosis is often not present until later stages of iron deficiency. It is important to note, however, that about 40% of the time, the anemia remains normocytic [1]. Serum ferritin levels are a marker of iron stores. Ferritin levels below 15 ng/mL are consistent with IDA, although, using 30 ng/mL as a cutoff may improve sensitivity [7]. Additionally, since ferritin is an acute phase reactant and often quite elevated in patients with chronic inflammatory conditions, a higher threshold is used to reflect IDA i.e. ferritin levels below 50 or 100 ng/mL in these patients. In patients with quiescent inflammatory bowel disease (IBD), for example, iron deficiency is defined as ferritin <30 ng/mL or transferrin saturation < 16%, whereas in IBD patients with active disease the serum ferritin cut off is 100 ng/mL [1, 8, 9].

Fecal Occult Blood Testing (FOBT)

As noted earlier, melena or hematochezia may be seen when a patient passes large volumes of blood (100 mL or more) from the GI tract. However, when less than 100 ml is passed, stool may be dark or appear normal. This is when fecal occult blood testing (FOBT) may be useful to identify suspected GI bleeding. Fecal occult blood tests start to become positive at a level of about 2 mL per day or higher, but the sensitivity increases considerably as the volume of fecal blood increases [8]. Testing for occult blood is often performed through guaiac-based stool tests, fecal immunochemical tests (FIT), and heme-porphyrin based tests.

Guaiac is a brown resin from the guaiacum tree that turns a blue color when it oxidized by the pseudoperoxidase activity of hemoglobin. Guaiac tests preferentially detect lower GI tract bleeding due to degradation of the hemoglobin that occurs in the upper GI tract. Nevertheless, there are a number of upper GI lesions that can be detected on guaiac based testing if enough blood loss is present [9].

Similarly, immunochemical testing is also sensitive and specific for lower GI tract bleeding, but not upper GI tract bleeding due to hemoglobin degradation. Immunochemical tests work by detecting human globin epitopes and thus, do not require dietary restriction and is less affected by concomitant medication use. Discontinuation of aspirin/NSAIDs is not needed as in other forms of testing. Additionally, only one stool sample is required as opposed to the three samples required for guaiac based FOBT. The heme-porphyrin assay which accurately measures the total stool hemoglobin by the porphyrin derived from heme through spectrofuorometric method, can be confounded by myoglobin, which is also found in red meats, making dietary restriction necessary. On the contrary, ingestion of

vitamin C, such as in fruits, fruit juices, or supplements, may cause false-negative results as vitamin C inhibits oxidation [10, 11].

Historically, the goal of FOBT was to detect microscopic bleeding in the GI tract and aid in the detection of colorectal neoplasia. Overuse of FOBT, especially in the inpatient setting, where it is inappropriately used for any anemia, has led to increased false positive tests [12]. Additionally, inadequate sampling (one instead of three) has led to inappropriate use in the outpatient setting with premature referral to invasive testing [13]. As noted earlier, in patients with IDA, a negative FOBT does not necessarily rule out GI bleeding, especially if located in the upper GI tract. The FOBT was falsely negative in 42% of patients with IDA who had lesions on upper endoscopy that were the likely the source of the bleed [14].

More information about FOBT is provided in Chap. 2.

Sources of Occult GI Bleeding

Occult GI bleeding can occur anywhere in the GI tract from the oropharynx to the anus and a source is found in approximately 60% of cases. The majority of patients (30–55%) end up having an upper GI source while 20–30% have a colorectal source. About 10% of patients have synchronous lesions in which there are both upper and lower GI lesions. In those patients in which the lesion is not found on EGD or colonoscopy, a thorough small bowel evaluation reveals the source in 30–50% of these patients [15, 16].

As summarized above, the causes of occult GI bleeding are commonly categorized by their location within the GI tract and usually divided into endoscopic areas: upper GI tract, small bowel, or lower GI tract. They can also be further classified by the different pathologic categories: neoplastic, vascular, inflammatory, genetic, or other as shown in Table 1.2 [5].

Non-Gastrointestinal Causes of Bleeding

The GI work up for iron deficiency anemia sometimes returns negative. Though this is a textbook on occult GI bleeding, it warrants special warning to the clinician that the source of the anemia still needs to be aggressively sought and may ultimately be an area anatomically close to the GI tract. Unseen bleeding from epistaxis, hemangiomas, or occult trauma to the nasal or oropharyngeal passage, for example, may result in ingestion of blood unbeknownst to the patient. As such, a thorough physical exam or referral to otolaryngology may end up finding the source. Rarely, history of blood from the oropharynx can be confused as hematemesis when in fact, it is from bleeding from the respiratory tract (hemoptysis) that the patient could be ingesting [17].

Table 1.2 Sources of occult Gl bleeding

Neoplastic	Vascular	Inflammatory	Genetic	Other
Carcinoma – esophageal, gastric, small bowel, colon Adenoma Polyposis syndromes Gastrointestinal stromal cell tumor (GIST) Kaposi sarcoma Lynphona Leiomyoma or leiomyosarcoma Carclnoic Lipoma	Vascular ectasias (at any site) Post-surgical (biopsy site, polypectomy, anastomotic bleeding) Anorectal disease (hemorrhoid, fissure) Diverticular bleed Gastric aAntral vascular ectasia (GAVE) Ischemia (i.e. ischemic colitis) Dieulafoy's lesion Cameron lesion Meckel's diverticulum Amyloidosis Gastrointestinal hemangioma Vasculitis	Aorto-enteric fistulas Inflammatory bowel disease (IBD) Erosive esophagitis Erosive gastritis Cameron lesion Colitis (including medication-induced) Ulcerative jejunitis from celiac disease Endometriosis Portal hypertensive gastropathy or enteropathy Varices (esophageal, gastric, small bowel) Ulcer (any site, including medication-induced)	Osler-Weber-Rendu sydrome Blue rubber bleb nevus syndrom Neurofibromatosis type I or II Gardner's syndrome Klippel-Trenaunay-Weber syndrome Ehlers-Danlos syndrome Hermans ky-Pudlak syndrome	**Infectious diseases:** Clostridioides difficile Cytomegalovirus Parasitic infection Helicobacter pylori Tuberculosis **Non-GI causes that can mimic GI bleeding:** Long-distance running Hemoptysis Oropharyngeal bleeding (i.e epistaxis) Gynecologic bleeding Factitious bleeding (self-induced)

[a]Lee and Laberge [42]
[a]Rockey [43]

Management

The Role of Thorough History and Physical

The differential diagnosis of GI bleeding is broad. Thus, a targeted approach based on the patient's symptoms, past medical history, family history, and physical exam may result in a swift and more efficient investigation.

Many patients with occult GI bleeding present with moderate to severe anemia on labs, but can be surprisingly asymptomatic due to the chronicity of the bleeding with adequate compensation. Thus, these patients may not present with the typical signs or symptoms of anemia, such as fatigue, weakness, and reduced exercise capacity. More subtle symptoms of chronic iron deficiency anemia include hair loss, hand and feet paresthesias, restless leg syndrome (often seen even in iron deficiency alone prior to the anemia), and in men, impotence. It may not be until severe anemia

with hemoglobin <7 mg/dl that the patient will finally begin to display more disconcerting symptoms such as pallor, headache or dizziness from hypoxia, tinnitus from the increased circulatory response, or dyspnea from high output cardiac failure [1].

A detailed history of gastrointestinal symptoms such as heartburn, dysphagia, odynophagia, recurrent nausea, vomiting, or prolonged anorexia should direct the clinician to an upper GI source. A history of severe reflux symptoms or difficulty swallowing may suggest esophagitis. Epigastric abdominal pain, burning in the epigastrium after eating, or intolerance of foods may suggest gastritis or gastric ulcers, especially in patients who have a history smoking, of overusing NSAIDs, or having a diet known to be associated with gastritis or ulcers. A history of alcoholism, especially with cirrhosis, could also be suggestive of peptic ulcer disease as well as premalignant colonic neoplasia [18]. Symptoms consistent with a lower GI source include a change in the stool caliber, diarrhea, constipation, lower abdominal pain. Parasitic infections can cause a constellation of non-specific symptoms including abdominal pain, flatulence, nausea, diarrhea, and signs of iron deficiency anemia. Exposure to typical water sources and foods prone to parasite ingestion or inoculation will be important.

Furthermore, a chronic overt GI bleed, such as recurrent variceal bleeding, may present as occult GI bleeding. These patients may have chronic melena that goes unnoticed or is ignored. The delayed presentation of an overt GI bleed will likely result in IDA. Patients with chronic liver disease may develop chronic GI bleeding and IDA from portal hypertensive gastropathy and gastric antral vascular ectasia (GAVE). Angiodysplasias may present as chronic GI bleeding due to frequent rebleeding and the presence of multiple lesions [19, 20].

Patients with red flag signs such as a history of unintentional weight loss or family history of malignancy may have a mass lesion, typically of the lower GI tract. It is important to remember that these patients may not have GI symptoms at all and, if they are above the age of 45–50 years old, colorectal cancer is at the top of the differential, especially if they have never had colorectal screening in the past. Additionally, a history of radiation or malignancy related treatment to an area of the GI tract might suggest mucosal injury as the source of bleeding, such as radiation proctitis.

Concurrent diagnosis of aortic stenosis and occult GI bleeding may suggest bleeding from acquired coagulopathy, known as Heyde's syndrome, in which the patient develops angiodysplasias [21]. Patients with end stage renal disease (ESRD) are also at risk of gastric vascular ectasias and colonic angiodysplasias, though the pathophysiology is not well understood [22]. The implantation of left ventricular assistive devices (LVAD) have an increased association with angiodysplasias as well [23]. A history of liver disease or portal hypertension might suggest varices or portal hypertensive gastropathy. Sometimes the diagnosis is not yet made, and the clinician must be vigilant for physical exam findings such as caput medusa, spider angiomas, or abdominal distention due to ascites, which will be the key to diagnosis.

A history of severe epistaxis may suggest a vascular lesion, especially when associated with telangiectasias of the lips, tongue, or palms. Multiple vascular

lesions might also indicate hereditary hemorrhagic telangiectasias, and a careful family history must be elicited. Blue or colored papules on the skin, in the right setting, may suggest blue rubber bleb nevus syndrome, which is a rare, severe, sporadically occurring disorder characterized by multiple venous malformations.

Special Populations

Special populations warrant a mention here to make sure that key sources of occult bleeding are not missed. Specifically, pre-menopausal women, patients less than 40 years old, particularly pediatric patients, and patients on anticoagulants.

Anticoagulant Use

Positive FOBT in patients on chronic antiplatelets, NSAIDs, or anticoagulation should not be attributed to medication use unless endoscopy is unrevealing. There are mixed data on whether antiplatelet, anticoagulants, and NSAIDs increase or decrease the positive predictive value or sensitivity of detecting colorectal neoplasms [24]. Ultimately, positive fecal occult blood tests, in patients taking either low-dose aspirin or warfarin, should be managed in the same fashion as patients not taking these medications [25].

Pediatric Patients

Many times, simple demographic data may help drive the work up. For example, in patients less than 40 years of age, small bowel tumors, inflammatory bowel disease, Dieulafoy's lesion, or Meckel's diverticulum (especially in the pediatric population) may be the likely etiology [26]. Bleeding in older patients tend to be from neoplasia or medication-induced GI complications, such as mucosal ulcers or gastropathy due to NSAIDs. Younger patients tend to have inflammatory lesions and are more prone to have bleeding from ulceration of a Meckel's diverticulum in the small bowel. The ulceration occurs in the distal mucosa and occurs due to acid secretion by ectopic gastric mucosa within the diverticulum [27]. Dieulafoy's lesions were named in 1898 by a French surgeon, and are submucosal arterial malformations that are difficult to diagnose as they are most commonly located in the small bowel [28]. In neonates, small bowel lesions would also include necrotizing enterocolitis. In infants, milk-protein allergy would also be of consideration. Other causes of small bowel bleeding in patients less than age 40 are seen in Table 1.3.

Table 1.3 Common occult GI bleeding in the small bowel based on age

Under age 40 years	Over age 40 years
Neoplasia (typically of small bowel)	Vascular ectasia
Inflammatory bowel disease (IBD)	Dieulafoy's lesions
Dieulafoy's lesions	Neoplasia
Meckel's diverticulum	NSAID-induced ulcers
Polyposis syndromes	Aorto-enteric fistula (if history of prior surgery)
	Small bowel varices
	Portal hypertensive enteropathy

Table adapted from Welli et al. [44]

Pre-Menopausal Women

IDA in pre-menopausal women is often due to heavy menses. As such, gynecologic sources of bleeding should be excluded before a full GI workup. However, women with GI symptoms and a positive FOBT or IDA warrant evaluation with EGD and colonoscopy for an occult GI bleeding source. In a study of 186 premenopausal women with a positive FOBT who underwent endoscopy, 23% had a clinically important lesion. These lesions were often in the upper GI tract and related to peptic ulcer disease (3%) or gastric cancer (3%). In these women, hemoglobin <10 g/dl, positive FOBT, and GI symptoms predicted clinically significant findings on endoscopy [29].

Clinical Approach to Occult GI Bleeding

The clinical approach to a patient with occult GI bleeding. or suspected occult GI bleeding will depend on the patient's age, clinical history, and whether the patient has a positive FOBT or IDA. It is important to assess the patient's stability, and formulate an effective diagnostic and treatment plan. We will go through the management of several patient populations based on their clinical presentations using the American College of Gastroenterology (ACG) clinical guidelines on small bowel bleeding from 2015, the American Gastroenterological Association (AGA) medical position on obscure GI bleeding from 2007, and the AGA Clinical Practice Guidelines on the Gastrointestinal Evaluation of Iron Deficiency Anemia from 2020 [2, 30].

The Patient with a Positive FOBT, But Without Iron Deficiency Anemia

If an asymptomatic patient has suspected GI bleeding with a positive FOBT and no IDA, then colonoscopy is recommended, especially if the patient is over 50 years [31]. The reason colonoscopy is preferred as a first step is because of the high risk of colonic carcinoma, the fact that upper GI sources of bleeding typically cause symptoms, and the high prevalence of false-positive FOBT and FIT. If the patient

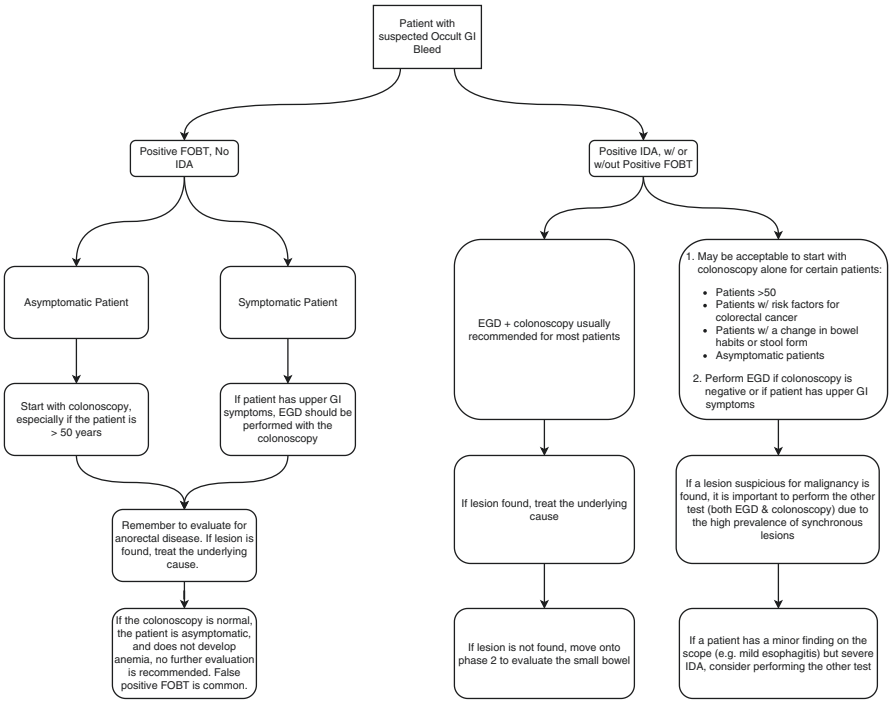

Fig. 1.1 Diagnostic algorithm for patients with suspected occult gastrointestinal (GI) bleeding with positive fecal occult blood test (FOBT) and/or positive iron deficiency anemia (IDA). EGD = esophagogastroduodenoscopy.

has upper GI symptoms, EGD should be performed along with the colonoscopy. If the colonoscopy is normal, the patient is asymptomatic, and does not develop anemia, then no further evaluation is recommended [Fig. 1.1] [2, 4, 31].

Since false positive FOBT is common, particularly with guaiac-based tests, testing error must be considered if the clinical scenario is inconsistent with bleeding. As guaiac-based tests rely on the pseudoperoxidase activity of hemoglobin, consumption of trace blood in red meats may cause a false-positive test. Similarly, foods that contain peroxidase, such as cruciferous vegetables (i.e. broccoli, cauliflower) can also cause a false positive. Swallowing blood from epistaxis or gingival bleeding may also produce a positive FOBT. Lastly, a positive FOBT may also be due to anorectal disease, including hemorrhoidal bleeding or the presence of a fissure [1, 12, 32]. A large study of asymptomatic patients found that the presence of hemorrhoids was an independent risk factor for false positive FIT results. Some studies have supported this finding, while others have shown no association [33, 34]. Hemorrhoids are rarely a cause of IDA, unless there is an overt bleed [35]. Given the disparities between studies, we recommend a colonoscopy in older patients with positive FOBT results to rule out more serious colorectal pathology even if the patient has known hemorrhoids. If the patient has hemorrhoids and a persistently positive FOBT after normal colonoscopy, then no further evaluation is warranted. If a younger patient has a positive FOBT, is asymptomatic, and does not have IDA or

risk factors for colorectal cancer, it is reasonable to observe the patient. Lastly, if the patient has hemorrhoids, positive FOBT, and IDA, then evaluation of the upper and lower GI tract is warranted per the algorithm below.

The Patient with Iron Deficiency Anemia +/– Positive FOBT

Patients with iron deficiency anemia not attributed to hematologic or malabsorption causes, particularly men and post-menopausal women warrant evaluation regardless of whether FOBT is positive or negative to rule out serious pathology. The most common etiologies of occult GI bleeding and resulting IDA in these patients include colonic carcinoma, mucosal injury from long term aspirin (or other nonsteroidal anti-inflammatory drug use), angiodysplasia, gastric carcinoma, peptic ulcer disease, esophagitis, H. pylori infection, GAVE, gastrectomy, and small bowel tumors [1]. Thus, patients with IDA and a positive FOBT often require both EGD and colonoscopy as an initial workup. In particular, IDA in men and postmenopausal women must be assumed due to GI blood loss and warrants evaluation with both EGD and colonoscopy [2, 31]. Additionally, premenopausal women without a history of menorrhagia and incidental finding of IDA or patients with IDA and concurrent GI symptoms should undergo both EGD and colonoscopy.

For certain patient populations, it is acceptable to start with either colonoscopy or endoscopy as the initial diagnostic test. Consider colonoscopy as the initial diagnostic test in a patient with IDA over 50 years old without any GI symptoms if they have risk factors for colorectal cancer such as a family history or a change in stool form or frequency. Consider EGD as the initial diagnostic test in a patient with upper GI symptoms, a history of NSAID use or abuse, heavy alcohol use or cirrhosis, or those with a history of developmental disability, or inability to express GERD symptoms. If one test is normal, it is reasonable to perform the other for a complete evaluation. EGD and colonoscopy may be performed in succession during on the same day for patient convenience, decreased sedation use, and cost reduction. Some physicians prefer to give the patient a bowel prep for a colonoscopy, and if the colonoscopy is normal, then perform the EGD next. The decision of whether to perform the second scope should be individualized based on patient findings. For example, if the severity of the IDA is not fully explained by the severity of the lesion (i.e. mild esophagitis seen with significant IDA), then a colonoscopy is reasonable to evaluate for a significant lower GI lesion since on average, 10% of patients will have synchronous lesions [2, 15, 31].

During the EGD, duodenal biopsies should be performed to rule out celiac disease. Of note, according to the ACG small bowel bleeding guidelines, celiac disease is no longer considered a cause of GI bleeding. Instead, the thought is that celiac disease causes iron deficiency anemia from malabsorption, not occult GI bleeding. However, in rare cases, ulcerative jejunitis, lymphoma, and adenocarcinoma can occur from celiac disease complications and result in small bowel bleeding [2]. Biopsies should also be performed in the colon, particularly in patients with diarrhea, as 50% of microscopic colitis have mild anemia [36].

Small Bowel Evaluation

If EGD and colonoscopy are normal, and the patient has severe IDA, persistent symptoms of small bowel lesions (diarrhea), or failure of IDA to correct with adequate replacement therapy, then an evaluation of the small bowel or second-look endoscopy is warranted [2, 31]. The most commonly used diagnostic tool for small bowel evaluation is a video capsule endoscopy (VCE), whereby a wireless camera in capsular form is ingested by the patient to help visualize portions of the small bowel inaccessible by EGD and colonoscopy. The diagnostic yield of VCE is 38–83% in patients with suspected small bowel bleeding [37]. Not every patient can undergo VCE, particularly those with stricturing Crohn's disease, clinical signs of obstruction, a history of radiation to the small bowel, certain motility disorders, and pregnant patients [38]. In these patients with contraindications to VCE, radiographic tests, such as computed tomographic enterography (CTE) can also be used [Fig. 1.2] [2]. Another drawback of VCE is its poor ability to localize a lesion in terms of guiding deep enteroscopy for intervention [2].

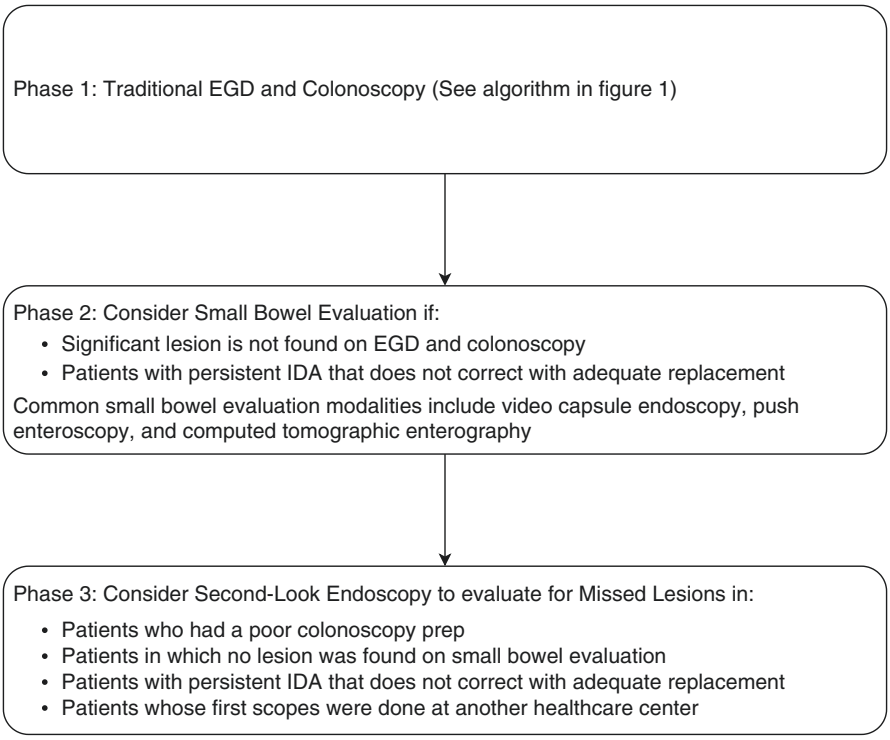

Fig. 1.2 Phases of diagnostic evaluation of patients with occult gastrointestinal (GI) bleeding EGD = esophagogastroduodenoscopy; IDA = iron deficiency anemia

Another commonly used diagnostic tool for the small bowel is push enteroscopy which has the benefits of intervention as well as better visualization of the proximal small bowel 45–90 cm distal to the ligament of Treitz. Push endoscopy has a diagnostic yield of 3–70% in cases of suspected small bowel bleeding [2]. However, most of the lesions found on push endoscopy are actually within reach of a traditional endoscope, which reiterates the importance of a careful first inspection of the upper GI tract with EGD and the importance of second-look endoscopy [39, 40]. Disadvantages of push enteroscopy include patient discomfort as compared to a traditional EGD and looping of the enteroscope in the stomach. Of note however, it actually offers a better view of the duodenum and proximal jejunum compared to the VCE. However, if push enteroscopy is normal, it is reasonable to move onto VCE for visualization of the more distal small bowel. With the advances in technology, there is now also single balloon, double balloon, and spiral enteroscopy which allow for examination of the full length of the small bowel. More details are discussed in the endoscopy chapter.

The Patient Who Warrants Second-Look Endoscopy/ Colonoscopy Due to Potential Missed Lesions

As noted earlier, second-look endoscopy is warranted to patients with refractory anemia for whom a comprehensive initial exam did not uncover the bleeding source. Endoscopy is an invaluable tool, but lesions are often missed. Studies have shown that 3.5% to greater than 30% of clinically significant non-small bowel lesions are missed on EGD, push enteroscopy, and colonoscopy that are incidentally detected by VCE. This means that these lesions were within reach of the traditional EGD and colonoscopes, but were missed.

Second-look entails repeating the EGD or colonoscopy or performing a push enteroscopy. The latter can be considered another form of second-look endoscopy, as it allows for direct visualization of the upper gastrointestinal much beyond the ligament of Treitz, particularly the distal duodenum and proximal jejunum which is challenging to see with VCE and out of reach of a traditional endoscope. Missed lesions occur more commonly in the lower GI tract than the upper GI tract. However, when the missed lesion is in the upper GI tract, it is most commonly found in the antrum. Cameron lesions can be missed in patients with a large hiatal hernia. Colorectal cancer can be missed in patients with a poor prep. Arteriovenous malformations or Dieulafoy's lesions can be missed if they are present in the gastroduodenum and may require a side view scope. Anal cancer can be missed if a rectal exam was not done or during rapid colonoscope insertion. Varices can be missed if they are deflated (as in under-resuscitated patients). Due to the high prevalence of these missed lesions, it may be worthwhile to repeat EGD and colonoscopy in a

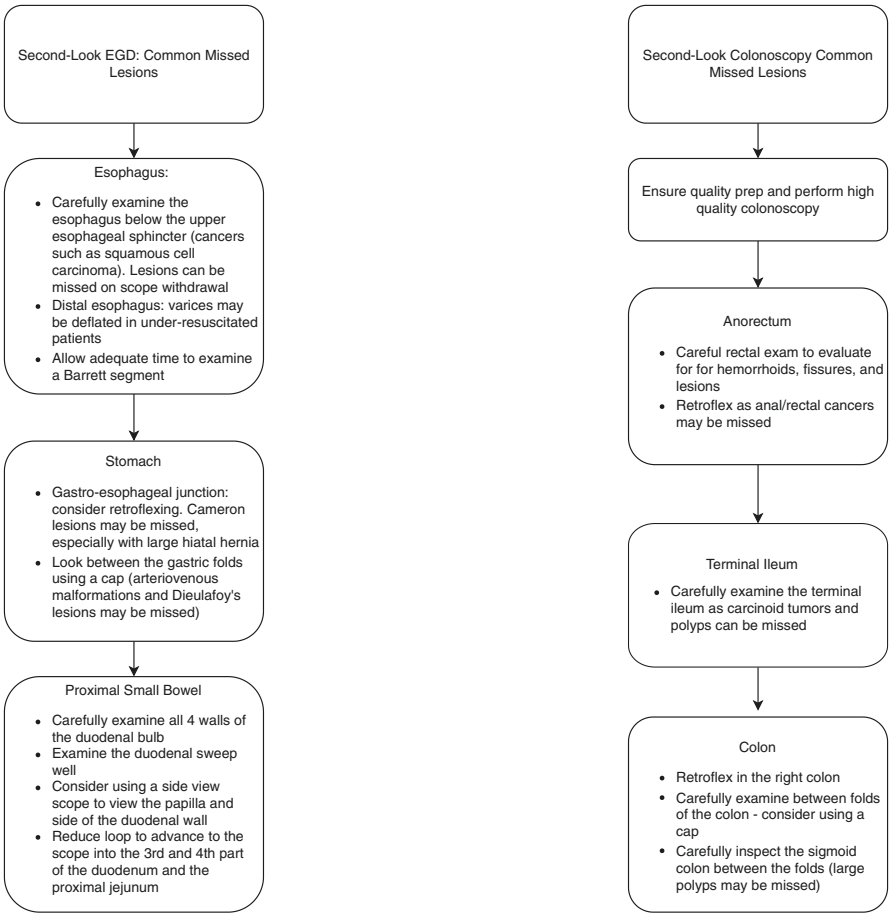

Fig. 1.3 Recommendations evaluation of missed lesions during second-look endoscopy. EGD = esophagogastroduodenoscopy

patient with persistent IDA that does not correct with adequate replacement and a positive FOBT, especially when the first examination was done at a different health-care center [41], [Fig. 1.3].

Subsequent chapters will delve into the specifics of screening tests, endoscopic evaluation, imaging, differential based on the sites of the lesion, management, and special populations.

Acknowledgments The authors thank Ms. Elizabeth Irish and the Albany Medical College Library for their contribution to this chapter.

Appendix 1

		Gastrointestinal bleeding	
		Occult – unseen by the patient and clinician	Overt – seen by the patient and clinician
SOURCE OF BLEED or PATHOLOGY	**Obvious**-positive EGD or colonoscopy (or small bowel testing*)	**Occult/obvious source**	Overt/obvious source
	Obscure-negative EGD, colonoscopy (or small bowel evaluation*) but patient continues to bleed (5% of all bleeds)	**Occult/obscure source**	Overt/obscure source

*Small bowel evaluation may include video capsule endoscopy and enteroscopy.
EGD: Esophagogastroduodenoscopy.

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