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Treatment for Iron Deficiency Anemia Associated With Heavy Menstrual Bleeding

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FAST FACTS

- Iron deficiency anemia (IDA) is a serious health problem that affects millions of women globally[1]
- Heavy menstrual bleeding (HMB) is one of the most common causes of IDA in women in North America[2]
- HMB-associated IDA is a common and under-appreciated condition[2,3]
- The health and quality-of-life (QoL) consequences of iron deficiency (ID) or IDA include fatigue,[4] decreased cognitive ability,[5,6] and impaired exercise capacity[7]
- When recognized, treatment of HMB-associated IDA should include addressing the underlying cause of HMB and correcting anemia with iron-repletion therapy[8,9]
- Both oral and intravenous (IV) iron are safe and effective FDA-approved treatments for IDA; IV iron is an option for patients unable to tolerate oral iron or achieve their treatment goals with oral therapies[9-15]
- Obstetrician/gynecologists are in a unique position, as both primary care providers for women and as experts who diagnose, treat, and when needed, refer patients for HMB-associated IDA[16]
- Proactively educating health care providers (HCPs) and patients about the frequency, implications, and appropriate treatment of HMB-associated IDA can help improve both their QoL and the clinical outcomes of therapy, including avoidance of red blood cell transfusion

DISCLOSURES

Dr. Boccia reports that he is a consultant to American Regent, Inc. and a consultant and speaker for Daiichi-Sankyo, Inc.
Dr. Friedman reports that he is a consultant to American Regent, Inc. and is a speaker for Daiichi Sankyo, Inc.
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Domestic and worldwide impact of HMB and iron deficiency and iron deficiency anemia in women

The International Federation of Gynecology and Obstetrics (FIGO) defines abnormal uterine bleeding (AUB) in nonpregnant women of reproductive age as intermenstrual bleeding or one or more abnormalities in frequency (too frequent or too infrequent), regularity (regular or irregular), duration (normal or prolonged), or volume (light, normal, or heavy) of menstrual flow.[8,17] A subcategory of AUB is the symptom of heavy menstrual bleeding (HMB), which is defined as excessive menstrual blood loss that interferes with a woman's physical, social, emotional, and material quality of life (QoL).[3,8,16,18]

The symptom of HMB is a common problem for women of reproductive age.[3,16,19] Survey-based studies report that at least 1 in 4 women will suffer from excessive menstrual blood loss during some point in their lives.[3,19,20] There is wide variability in reporting of HMB, which has led to a likely underestimation of its prevalence.[2,3] There are several reasons for the underreporting of HMB. First, definitions of the symptom of HMB have varied and until recently were frequently based on quantification of blood loss in a way that was impractical for clinical use.[3] Even when present, the symptom of HMB appears to be underrecognized by patients as they may not consider their blood loss to be excessive[2,3,18,21] or even urgent.[22] Many women do not report excessive bleeding to their families,[19] teachers, employers,[23] or HCPs.[2,3] Furthermore, when reported by patients, the symptom of HMB often is minimized or entirely dismissed by HCPs.[2,3] Reasons for not seeking medical attention may include views about fertility, ignorance of noninvasive treatment options and medical costs, and hesitancy to discuss symptoms.[2,22] Consequently, an appropriate diagnosis is likely undercoded in large population databases, a circumstance that would result in an inaccurate reflection of prevalence.[24]

Women with HMB frequently have iron deficiency anemia (IDA).[3,25] Women with HMB-associated IDA experience decreased physical and emotional QoL.[2,3,29] Anemia is particularly problematic when women select surgical interventions for the treatment of their chronic AUB, and in particular, when the symptom is HMB. Data from 12,836 women undergoing surgical procedures in the American College of Surgeons National Surgical Quality Improvement Program demonstrate that operative morbidity, mortality, and hospital length of stay are increased when surgery is performed on women with hemoglobin (Hb) <11 g/dL.[30] These outcomes appear to be unaltered by perioperative blood transfusions, which patients with preoperative anemia are more likely to receive.[30]

Some estimates reveal that as many as 25% of women with HMB also have anemia.[3,22] HMB-associated anemia can have negative economic and clinical implications. The economic impact of the symptom of HMB includes lost work productivity[23,31,32] and increased health care resource utilization.[22,32,33] In 2007, the overall cost of AUB on the US health care system was estimated to be at least $37 billion.[2] One study from 2002 estimated that women with HMB were about 75% as likely to be present at work compared with those without the symptom, and burdened with additional annual health care costs of $2,291 per patient.[32] A National Health Interview Survey found that increased menstrual bleeding resulted in annual work loss of $1,692 per woman.[31]

The are several clinical implications for ID and IDA in nonpregnant and pregnant women as well as potential complications in neonates, including cognitive and behavioral abnormalities. Maternal IDA is associated with developmental deficits including lower birth weight, possible increased risk for preterm delivery, and disturbed postpartum maternal–infant interactions.[34,35] Studies in nonpregnant women have shown the adverse clinical impact of both ID and IDA on physiologic functions resulting in fatigue,[4] decreased cognitive ability,[5,6] and impaired exercise capacity.[7]

TABLE 1 Key components of iron metabolism

Component	Function	Dosing and administration
Hepcidin[9,25,26]	Negative regulator	A peptide that negatively regulates intestinal iron absorption and release from storage macrophages and enterocytes into systemic circulation
Ferritin[9,26,27]	Storage	The principal iron storage protein; ubiquitous but concentrated in the liver; serum ferritin reflects iron stores in individuals without chronic inflammatory disease
Ferroportin[9,25,26]	Export	An iron export protein located on cell membranes that transfers iron from enterocytes and macrophages to the systemic circulation where it can be bound by transferrin and carried to sites of utilization
DMT1[26,28]	Iron transport /Uptake	The major iron transporter of dietary iron into enterocytes and contributes non-heme iron uptake
Transferrin[25,26]	Iron transport /Uptake	An iron-binding protein responsible for transporting iron throughout the body

Abbreviation: DMT1, divalent metal transporter 1.

Iron physiology and the pathogenesis of ID and IDA

Although a comprehensive review of iron metabolism is beyond the scope of this article, there are a number of important components described here that provide the context necessary for clinicians to understand the rationale for contemporary diagnostic and therapeutic strategies for IDA. More than two-thirds of the body's iron content is incorporated into Hb in developing erythroid precursors and mature red blood cells (RBCs).[28] However, iron is

essential for maintaining many other bodily functions, including respiration, energy production, DNA synthesis and repair, myocyte utilization of myoglobin, and cell proliferation.[25]

Iron metabolism is tightly regulated.[25] In nonmenstruating women, about 1 to 2 mg of iron is provided by dietary absorption in the duodenum, and equal amounts are lost via unregulated loss from bodily fluids and epithelial desquamation.[25,28] Systemic regulation is controlled through dietary intake, and iron release from recycling macrophages and hepatocytes. Maintaining appropriate iron levels in cells and tissues is necessary for the performance of these biological functions.[3,25]

Multiple regulatory factors control appropriate absorption, uptake, and recycling of iron, which collectively maintain iron homeostasis (**TABLE 1**).[9,25,27,36] Hepcidin is a regulatory protein manufactured in the liver with properties that include control of the absorption and release of iron.[27] For example, hepcidin targets ferroportin for degradation, which impairs the flow of iron from cells into the systemic circulation.[9] Elevated levels of hepcidin appropriately decrease iron absorption with increasing levels of iron in the plasma and liver; however, such levels also are increased in inflammatory conditions, renal disease, and cancer, thus adversely affecting iron metabolism.[27,36] Release of hepcidin has been described in association with daily oral iron administration, a circumstance that has potential clinical implications when designing ideal oral iron replacement regimens (see "*Treating the cause of the HMB*" on page S6).[9,27]

Of the body's iron, one-fourth is bound to ferritin, an intracellular glycoprotein that can be measured in serum.[26,27] Serum ferritin is generally an indicator of iron stores and, consequently, low ferritin levels are usually indicative of ID in the absence of inflammation.[25] The utility of ferritin measurement diminishes in those with chronic conditions such as kidney or inflammatory bowel disease (IBD).[27] Other key molecular components of iron physiology include ferroportin and transferrin.[25] Ferroportin is a transmembrane protein that exports iron from cells like enterocytes and macrophages into the circulation; whereas transferrin is the iron-binding protein primarily responsible for systemic iron transport.[25]

Anemia is a decrease in Hb level with a corresponding reduced quantity of erythrocytes that typically display a spectrum of morphological changes.[25] The threshold for diagnosing anemia in women is Hb <12 g/dL.[25] There are many causes of anemia, including cancer, B_{12} or folate deficiencies, and hemolysis; however, ID is the most common cause and accounts for approximately 50% of cases worldwide.[1,25,29] The causes of IDA are multifactorial and can include poor iron absorption due to inflammatory conditions (eg, chronic kidney disease, IBD, heart failure), an iron-poor diet, bleeding in the intestinal tract, and HMB.[25,29] Individuals with ID have insufficient iron to meet the body's biological requirements. Functional ID occurs when there are adequate iron stores, but insufficient mobilization of erythroid iron despite increased demand.[25] Absolute ID occurs when the iron stores are depleted; when severe enough, erythropoiesis is inhibited.[27] Absolute ID can occur when there is excessive blood loss such as in the setting of HMB.[27]

ID is clinically distinct from anemia (ID can occur without anemia and vice versa).[25] IDA, a late consequence of ID, occurs when the anemia is caused by depressed levels of total body iron.[25,36]

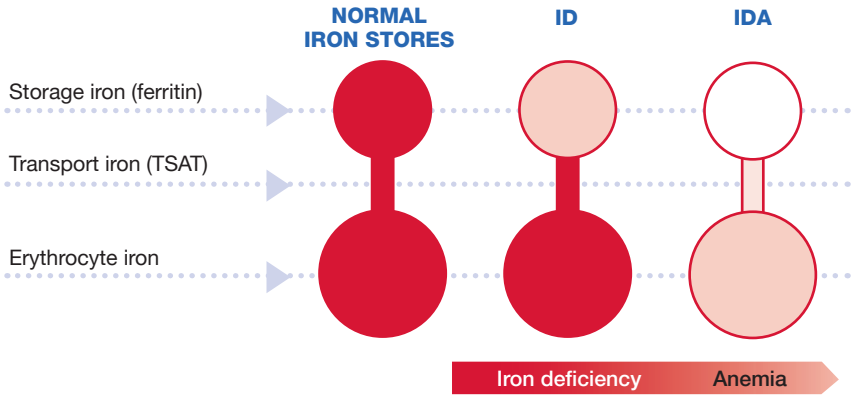
Distinguishing ID, IDA, and other causes of anemia are vital to appropriate clinical decision making. **FIGURE 1** illustrates the differences between normal iron status, ID, and IDA using key assessment parameters.[37] Although the causes of ID and IDA are multifactorial, we focus on iron depletion due to blood loss through the symptom of HMB.

HMB and IDA: Signs, symptoms, and laboratory evaluation

FIGURE 2 outlines the diagnostic workup of patients with HMB suspected of having ID or IDA. Regardless of the presence of symptoms, patients should be treated to reduce or prevent continued iron loss. Patients should be evaluated to determine the cause of HMB using a structured approach based on the 2 FIGO AUB systems (**FIGURE 3**).[8,17]

The elements of FIGO AUB System 1 require obtaining a detailed menstrual history that includes cycle length in days (normal is 24–38 days); regularity (shortest to longest cycle variation normally ≤7–9 days); duration (>8 days is prolonged); and volume as

FIGURE 1 Iron parameters[25,37]

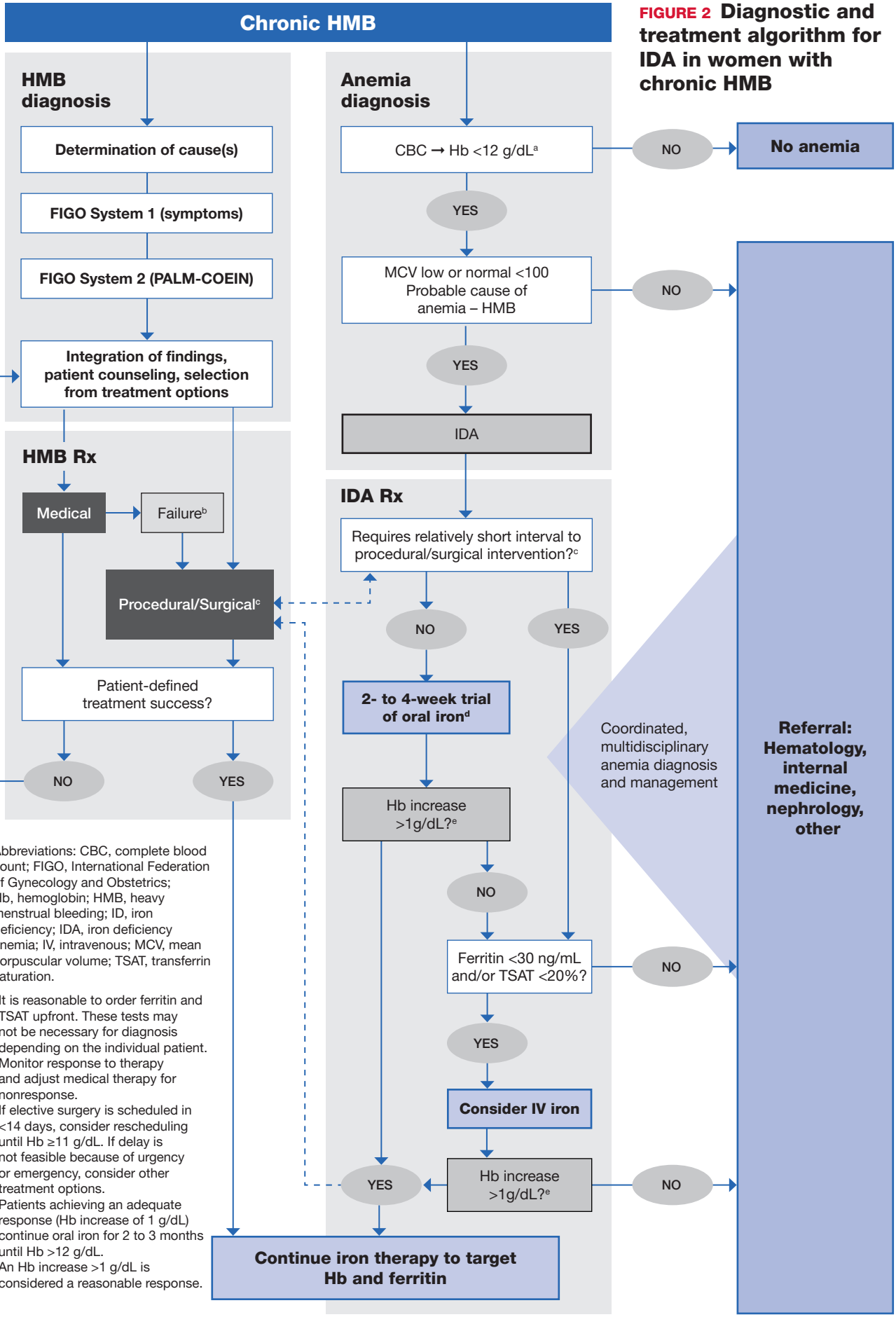


Plasma ferritin (ng/mL)	20–200	<30	<10
TSAT (%)	>16 to <45	≥16	<16
Erythrocyte morphology	Normal	Normal	Normal/ Microcytic hypochromic

Abbreviations: ID, iron deficiency; IDA, iron deficiency anemia; TSAT, transferrin saturation.

Adapted from Crichton R, Danielson BG, Geisser P. *Iron therapy with special emphasis of IV administration*. 4th ed. Bremen, Germany: Uni-Med Verlag AG; 2008.

FIGURE 2 Diagnostic and treatment algorithm for IDA in women with chronic HMB



Abbreviations: CBC, complete blood count; FIGO, International Federation of Gynecology and Obstetrics; Hb, hemoglobin; HMB, heavy menstrual bleeding; ID, iron deficiency; IDA, iron deficiency anemia; IV, intravenous; MCV, mean corpuscular volume; TSAT, transferrin saturation.

[a] It is reasonable to order ferritin and TSAT upfront. These tests may not be necessary for diagnosis depending on the individual patient.
[b] Monitor response to therapy and adjust medical therapy for nonresponse.
[c] If elective surgery is scheduled in <14 days, consider rescheduling until Hb ≥11 g/dL. If delay is not feasible because of urgency or emergency, consider other treatment options.
[d] Patients achieving an adequate response (Hb increase of 1 g/dL) continue oral iron for 2 to 3 months until Hb >12 g/dL.
[e] An Hb increase >1 g/dL is considered a reasonable response.

determined by the patient.[8] Volume that is excessive to the point that it interferes with QoL is considered heavy, even if it does not meet the traditional research definition of 80 mL per menses and regardless of the presence or absence of ID or IDA.[8] The menstrual history is not adequately evaluated by answers such as "my periods are normal," or "regular" as many women with HMB may have normalized their bleeding volume based on previous misleading family or HCP feedback, and have compensated for excessive bleeding with lifestyle-altering behaviors such as social avoidance, use of large pads, and alterations in attire. The terms *regular* or *irregular* can have a spectrum of meanings for women beyond those perceived by a provider. Therefore, it is better to identify the typical range of cycle length and period duration in days. Even if a woman believes her flow is normal, but her medical history suggests it is excessive, an evaluation should be initiated to assess her Hb level.[8]

The System 2 investigation is, in large part, directed by the System 1 evaluation. However, for those with normal cycle length, regularity, and HMB, the investigator should liberally use appropriate uterine imaging techniques and evaluate for coagulopathy as indicated by the structured history.[8,17]

The signs and symptoms of IDA may depend on the severity of iron depletion. Patients with mild to moderate IDA may be asymptomatic. When symptoms do occur, they can range from mild to severe and may include headache, fatigue, pica, weakness, exertional dyspnea, hair loss, brittle nails, cold insensitivity, and restless leg.[26,36] A diagnostic challenge of IDA is that many of its signs and symptoms also occur in patients with other types of anemia.

The diagnosis of IDA is laboratory-based and comprises measurements of Hb, serum ferritin, and transferrin saturation (TSAT).[29] An initial complete

FIGURE 3 The 2 FIGO systems for normal and abnormal uterine bleeding symptoms and classification of causes of abnormal uterine bleeding in the reproductive years[8]

A: FIGO AUB System 1.
The system for definition and nomenclature.

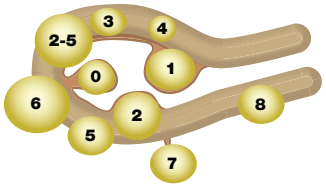
Parameter	NORMAL	ABNORMAL	☑
Frequency	Absent (no bleeding) = amenorrhea		☐
		Infrequent (>38 days)	☐
	Normal (≥24 to ≤38 days)		☐
		Frequent (<24 days)	☐
Duration	Normal (≤8 days)		☐
		Prolonged (>8 days)	☐
Regularity	Normal or "Regular" (shortest to longest cycle variation: ≤7–9 days)[a]		☐
		Irregular (shortest to longest variation: ≥8–10 days)[a]	☐
Flow Volume (patient determined)	Light		☐
	Normal		☐
		Heavy	☐
Intermenstrual Bleeding (IMB) Bleeding between cyclically regular onset of menses	None		☐
		Frequent (<24 days)	☐
		Cyclic (Predictable) – Early Cycle	☐
		Cyclic (Predictable) – Mid Cycle	☐
		Cyclic (Predictable) – Late Cycle	☐
Unscheduled Bleeding on Progestin ± Estrogen Gonadal Steroids (birth control pills, rings, patches, or injections)	None		☐
		Frequent (<24 days)	☐
		Cyclic (Predictable) – Early Cycle	☐
		Cyclic (Predictable) – Mid Cycle	☐
		Cyclic (Predictable) – Late Cycle	☐

B: FIGO AUB System 2.
The PALM-COEIN system for classification of causes of AUB.

- **P**olyp
- **A**denomyosis
- **L**eiomyoma → **S**ubmucous; **O**ther
- **M**alignancy & hyperplasia
- **C**oagulopathy
- **O**vulatory dysfunction
- **E**ndometrial
- **I**atrogenic
- **N**ot otherwise classified

Leiomyoma subclassification system

SM – Submucous	**0**	Pedunculated intracavitary
	1	<50% intramural
	2	≥50% intramural
	3	Contacts endometrium; 100% intramural
O - Other	**4**	Intramural
	5	Subserosal ≥50% intramural
	6	Subserosal <50% intramural
	7	Subserosal pedunculated
	8	Other (specify eg, cervical, parasitic)



Hybrid leiomyomas (impact both endometrium and serosa)

Two numbers are listed separately by a hyphen. By convention, the first refers to the relationship with the endometrium and the second refers to the relationship to the subserous. One example is shown here.

2-5
Submucous and subserous, each with less than half the mean maximal diameter in the endometrial and peritoneal cavities, respectively.

Abbreviation: FIGO, International Federation of Gynecology and Obstetrics.

[a]The available evidence suggests that, using these criteria, the normal range (shortest to longest) varies with age: 18–25 y, ≤9 d; 26–41 y, ≤7 d; and for 42–45 y, ≤9 d.

blood count (CBC) should be ordered to determine Hb levels. If the patient has Hb levels ≥12 g/dL, then she does not have anemia but may have ID.[25] If the Hb is <12 g/dL,ferritin and TSAT levels should be obtained. Serum ferritin levels <10 ng/mL (or creatinine clearance) and TSAT<16% are consistent with IDA.[9] Microcytosis also can be an indicator of IDA, so if Hb levels are <12 g/dL and there is microcytosis, ferritin and TSAT should be measured.[9] Depending on the patient's clinical scenario, it may be appropriate to order folate, B_{12}, and total iron-binding capacity to distinuish IDA from other causes of anemia.

Treatment recommendations for women with HMB-associated IDA

Treating the cause of the HMB

Women with HMB and IDA require a combined approach of medical and surgical measures aimed at cessation or reduction in blood loss of uterine origin and repletion of iron stores (**FIGURE 2**). For women with the symptom of HMB, the FIGO-based evaluation will have identified one or a combination of the potential causes found in System 2, the PALM-COEIN diagnostic system.[8,17] Depending on the identified cause or causes, medical therapy can promptly and effectively reduce or stop HMB. In many cases, medical therapy results in amenorrhea, and, even if surgery is ultimately chosen, will facilitate attaining an Hb level commensurate with the optimal reduction in perioperative morbidity without the need for blood transfusion.

Examples of medical therapies directed at the cause include use of nonsteroidal anti-inflammatory drugs, tranexamic acid, combined hormonal contraceptives, and progestin-only methods such as the levonorgstrel-releasing intrauterine system.[38,39] For attaining amenorrhea, the administration of a gonadotropin-releasing hormone agonist has been shown to facilitate the repletion of iron stores and is appropriate at least for women planning surgery.[40] Attaining preoperative amenorrhea is an important consideration for those women with IDA who select procedural approaches to the treatment of the cause of their HMB. This may be due to ineffectiveness or intolerance or, in the case of submucous leiomyomas, because of a short-term desire for fertility.

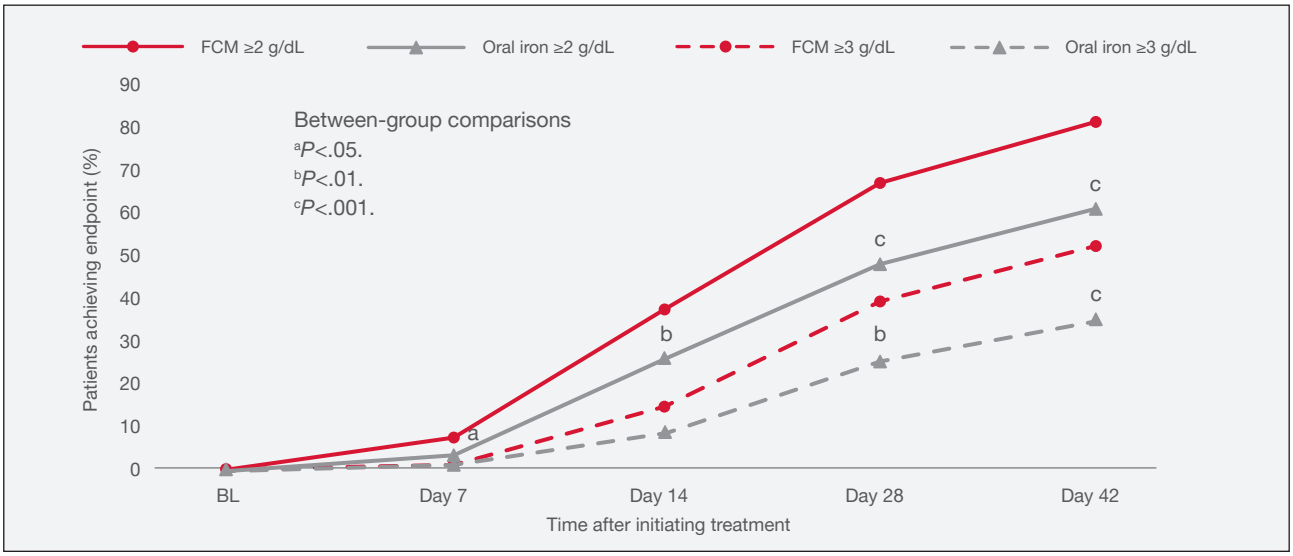
Treating IDA

Rarely, blood transfusion may be required in specific cases of acute hemorrhage and hemodynamic instability. The first-line treatment option for IDA is orally administered iron because it is usually safe, inexpensive, and readily available. Patients taking oral iron should be monitored periodically to ensure compliance and that the approach is both effective and well tolerated.

Clinicians should be aware of the potential challenges with oral iron. First, 20% to 40% of patients taking oral iron may experience side effects, including nausea, vomiting, constipation, and an undesirable metallic taste.[9,25,41] Anticipating gastrointestinal problems, many physicians will routinely recommend stool softeners when they prescribe oral iron. The frequency of side effects rises with increasing dose. The reported adherence rates for oral iron therapy range from 40% to 60%.[41] As some patients will tolerate one oral formulation better than others, it is reasonable to consider alternating formulations if iron intolerance is an issue.

A real problem is that daily multidose oral iron therapy increases hepcidin levels, thereby decreasing iron absorption.[42] Historically, the recommended daily dose comprised 150 to 200 mg of oral elemental iron;

FIGURE 4 Rapid IV is more effective than oral iron therapy in correcting anemia and replenishing iron stores[10]



174 anemic women (Hb ≤10 g/dL) within 10 days postpartum received either IV FCM (≤1,000 mg over 15 minutes, repeated weekly to achieve a total calculated replacement dose) or ferrous sulfate ($FeSO_4$) 325 mg orally 3 times daily for 6 weeks. Hb was evaluated at intervals for the following 42 days.

Abbreviations: BL, baseline; FCM, ferric carboxymaltose; Hb, hemoglobin; IV, intravenous.

Adapted from Van Wyck DB, et al. *Transfusion.* 2009;49:2719-2728.

however, recent data from 2 open-label, randomized controlled trials strongly suggest that absorption of iron may be enhanced by the use of single doses on alternate days.[42,43] Follow-up at the end of a 2-week trial will guide further recommendations. Patients achieving increased Hb (≥1 g/dL over 2 weeks) should continue oral iron to the target Hb (≥12 g/dL), ferritin (≥30–50 µg/L), and TSAT (>20%).[9,25,44]

Intravenous (IV) iron is an option for patients who do not achieve the Hb target with oral iron (either due to intolerance or inadequate response) or when rapid repletion is necessary (eg, short interval to surgery and severe IDA not requiring transfusion). A 2 g/dL increase in Hb is more likely within 4 weeks of starting IV iron than with orally administered iron. In patients with HMB-associated IDA, rapid administration of large doses of IV iron has been shown to be more effective than oral iron therapy in correcting anemia and replenishing iron stores (**FIGURE 4**).[10]

When selecting an IV iron agent, the provider should consider the risk–benefit profile of IV iron products. Historically, the most severe risk is anaphylaxis, an adverse event generally related to high-molecular-weight iron dextran products, now no longer available.[45] The risk for anaphylaxis has been greatly diminished with the development of newer, low-molecular-weight and non–dextran-containing IV iron formulations that have been approved specifically for IDA (**TABLE 2**).[11-15] Some IV iron preparations require fewer infusions and can replenish iron stores in 1 or 2 doses, an approach that reduces the number of visits, thereby decreasing office or institutional utilization.

Follow-up/Monitoring

Follow-up for the woman with the symptom of HMB and the diagnosis of IDA can be complicated. If the patient has acute HMB, it will be necessary to have short-term follow-up to determine response, and the need for potential alternate therapy if the therapeutic effect is inadequate. For those with chronic HMB, such as AUB-A, -C, -O, or -E, it may take several weeks to months to determine the impact of medical interventions. Consequently, follow-up regimens are dependent on cause. However, monitoring therapy for IDA is separate and should follow a prescribed approach.

Regular follow-up for patients prescribed iron therapy to treat IDA is required to assess efficacy and tolerability. The frequency of monitoring after initiating therapy for IDA depends on several factors, including whether the underlying cause of anemia was corrected, the baseline iron levels, and the selected treatment. All patients should be advised to immediately report the following causes of intolerance to their physician: nausea, black stools, diarrhea, constipation, vomiting, and abdominal discomfort.

Attaining a normal Hb is the primary treatment target of iron replacement therapy for IDA. As previously stated, patients on oral therapy should be considered for a short-interval follow-up in about 2 weeks to determine tolerance and response to therapy.[44] Such visits should include a CBC and laboratory assessments of iron parameters as well as symptom and compliance evaluation. For women, complete correction of Hb is a level that is 12 g/dL. If the patient does not achieve a 1 g/dL increase in iron in the first 2 weeks, she is unlikely to reach the desired target. When the patient on oral iron replacement fails to reach the short-term target, the clinician should identify potential reasons, which typically include the wrong dose or administration schedule, difficulties with absorption, and intolerance due to undesirable side effects or continued blood loss.[29] If there is intolerance to iron, and changing formulations is unsuccessful, IV iron therapy should be selected. In all patients, iron therapy (either IV or oral) should be continued beyond normalization of Hb levels and until the iron stores are replete.

Patients on IV therapy do not necessarily require less frequent follow-up. The frequency will depend on the clinical scenario and whether short interval treatment was initiated for

TABLE 2 IV iron formulations currently available in the United States[11-15]

Preparation	Product name (approval year)	Dosing and administration
Iron dextran[a,b]	INFeD (1974)	Test dose; slow infusion <50 mg/min; 100 mg/dose
Ferric gluconate in sucrose	Ferrlecit (1999)	125 mg slow infusion/injection
Iron sucrose	Venofer (2000)	Slow infusion 100–200 mg
Ferumoxytol[a]	Feraheme (2009)	510 mg over 15+ minutes
Ferric carboxymaltose	Injectafer (2013)	For patients >50 kg (110 lb): 750 mg either as a slow IV push (100 mg/min) or an IV infusion over 15+ minutes For patients <50 kg (110 lb): Injectafer can be administered in 2 doses separated by at least 7 days with each dose given as 15 mg/kg body weight

Abbreviation: IV, intravenous.

[a]FDA-approved prescribing information contains a black box warning on anaphylactic-type reactions, including fatalities, which have followed the parenteral administration of iron dextran injection.

[b]FDA approved for iron deficiency and not specifically indicated for iron deficiency anemia.

impending surgery or severe IDA. Patients who do not respond to IV therapy should be referred to colleagues in hematology, internal medicine, or nephrology for further evaluation and coordinated anemia management.

Once the desired response is obtained, prevention strategies should be considered in the context of the patient's clinical situation. For example, if there has been a medical or surgical correction of the HMB symptoms, the clinician should evaluate the need for further iron supplementation or therapy. For patients with a questionable HMB result, or for those resistant to HMB-related therapy, prevention strategies for reoccurrence of IDA include a regular follow-up schedule commensurate with response to HMB therapy and response to iron replacement.

Summary and future recommendations

The assessment of iron status, diagnosis of IDA, and treatment of both the underlying cause of HMB and associated ID involve a multidisciplinary approach that often begins with the obstetrician/gynecologist. Currently, there are no guidelines created or endorsed by US obstetrical and gynecological societies or organizations that focus on the management of IDA in patients with the symptom of HMB. Appropriately designed, evidence-based guidelines are urgently needed to address diagnosis and treatment for the underlying cause of HMB, appropriate treatment options for IDA, and appropriate follow-up. Such guidelines should include recommendations for transition from oral to IV iron, identification of possible causes of nonresponse to IV iron, and directions for gynecologic referral to hematologists or other appropriate specialists. The authors hope this article has provided the obstetrician/gynecologist with new insights into IDA and its relationship to AUB in general, including the often-normalized symptom of HMB, as well as newer and safer therapies for the repletion of iron stores. They also urge societies such as the American College of Obstetricians and Gynecologists to develop interdisciplinary, evidence-based clinical practice guidelines to optimize care of patients with HMB and associated ID and IDA. ■

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