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Iron Deficiency Anemia in Adults: From Diagnosis to Treatment - A Practical Clinical Review

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Abstract **Review Article**

Iron deficiency anemia (IDA) is among the most frequently encountered hematological disorders in adult clinical practice. Despite its high prevalence and generally effective treatment, IDA should not be considered an isolated laboratory abnormality because it often reflects an underlying disorder requiring identification and management. Chronic gastrointestinal or gynecological blood loss, impaired gastrointestinal absorption, increased physiological requirements, and insufficient iron intake represent the principal mechanisms of iron deficiency. Diagnosis requires integration of hemoglobin concentration, red-cell indices, serum ferritin, transferrin saturation (TSAT), and the clinical context. Ferritin is the most useful marker of iron stores in uncomplicated patients but may be misleading in inflammation, chronic kidney disease (CKD), malignancy, infection, and liver disease. Oral iron remains appropriate first-line therapy for many stable adults, with once-daily administration preferred and alternate-day dosing useful in selected patients with intolerance. Intravenous iron is appropriate when oral therapy is ineffective, poorly tolerated, inadequately absorbed, or when rapid repletion is required. This narrative clinical review summarizes contemporary evidence regarding diagnosis, etiological evaluation, oral and intravenous treatment, monitoring, and treatment failure, with special attention to gastrointestinal investigation and CKD.

Keywords: Iron deficiency anemia; ferritin; transferrin saturation; oral iron; intravenous iron; chronic kidney disease; gastrointestinal bleeding.

1. INTRODUCTION

Iron deficiency represents a progressive reduction in available body iron. Depletion of storage iron precedes iron-restricted erythropoiesis, and anemia develops when iron supply becomes insufficient to sustain normal hemoglobin synthesis. Iron deficiency may cause fatigue, reduced exercise capacity, cognitive symptoms, pica, and restless legs symptoms even before severe anemia develops.

The diagnosis of IDA should be regarded as the beginning rather than the end of the clinical evaluation. In adults, particularly men and postmenopausal women, unexplained IDA can be the first manifestation of clinically important gastrointestinal disease. The clinician must therefore establish both the presence of iron deficiency and its underlying cause. This review provides a practical framework for diagnosis, etiological investigation, iron replacement, monitoring, and management of special populations, including patients with CKD.

2. METHODS OF LITERATURE REVIEW

This narrative review was developed using targeted searches of PubMed and guideline repositories for English-language guidelines, reviews, randomized trials, and clinically relevant consensus statements concerning adult iron deficiency and IDA. Priority was given to major professional-society guidance, including the American Gastroenterological Association (AGA), British Society of Gastroenterology (BSG), European Hematology Association-associated recommendations, and kidney disease: Improving Global Outcomes (KDIGO), together with recent high-quality reviews and pivotal studies of oral and intravenous iron. Searches emphasized publications from 2020 through August 2026, while older landmark studies were retained when they informed current practice. Because this is a narrative review rather than a systematic review, no formal risk-of-bias assessment or meta-analysis was performed.

3. Etiology and Risk Factors

Iron deficiency develops when iron losses or physiological requirements exceed intestinal absorption. Chronic gastrointestinal blood loss may arise from peptic ulcer disease, erosive gastritis, gastrointestinal malignancy, colorectal polyps, inflammatory bowel disease, angiodysplasia, or medication-associated mucosal injury. NSAIDs, antiplatelet drugs, and anticoagulants may contribute to or reveal gastrointestinal bleeding.

Heavy menstrual bleeding is a major cause in premenopausal women. Malabsorption may occur with celiac disease, bariatric surgery, gastric resection, atrophic gastritis, inflammatory bowel disease, or disorders affecting the proximal small intestine. Increased requirements occur during pregnancy and recovery from substantial blood loss. Low intake of bioavailable iron may contribute, but dietary deficiency alone should not automatically be accepted as the cause of new adult IDA without appropriate assessment.

4. Clinical Presentation

Symptoms depend on the severity and chronicity of anemia and on cardiopulmonary reserve. Common manifestations include fatigue, weakness, dyspnea on exertion, palpitations, dizziness, headache, and reduced exercise tolerance. More characteristic features of iron deficiency include pica, restless legs symptoms, glossitis, angular cheilitis, brittle nails, and koilonychia. Slowly progressive anemia may produce relatively few symptoms despite substantially reduced hemoglobin.

5. Diagnostic Evaluation

Established IDA commonly produces microcytic, hypochromic anemia with reduced hemoglobin, reduced mean corpuscular volume (MCV), reduced mean corpuscular hemoglobin, and increased red-cell distribution width. However, early iron deficiency may be normocytic; a normal MCV does not exclude IDA. Microcytosis also requires consideration of thalassemia trait and anemia associated with chronic inflammation.

Serum ferritin is the most useful single biochemical marker of body iron stores in uncomplicated patients. The AGA recommends a ferritin cutoff of <45 ng/mL rather than <15 ng/mL when diagnosing iron deficiency in patients with anemia [1]. Ferritin is an acute-phase reactant and may be normal or elevated in infection, chronic inflammation, CKD, malignancy, and liver disease. Transferrin saturation (TSAT), calculated as serum iron divided by total iron-binding capacity multiplied by 100, provides complementary information regarding circulating iron availability.

Additional testing should be individualized and may include a peripheral blood smear, reticulocyte count, C-reactive protein, vitamin B12, folate, renal and liver function, thyroid-stimulating hormone, celiac serology, and hemoglobin electrophoresis. Mixed etiologies are common, particularly in older adults and patients with chronic disease.

6. Determining the Underlying Cause and Gastrointestinal Evaluation

History should address melena, hematochezia, dyspepsia, change in bowel habit, abdominal pain, unintentional weight loss, menstrual bleeding, NSAID use, antiplatelet or anticoagulant therapy, blood donation, dietary history, previous gastrointestinal surgery, and family history of gastrointestinal malignancy.

AGA guidance recommends bidirectional endoscopy in asymptomatic men and postmenopausal women with IDA and suggests the same approach in asymptomatic premenopausal women, with individualized decision-making [1]. After negative bidirectional endoscopy and no other identifiable etiology, noninvasive testing for Helicobacter pylori is suggested; celiac serology is appropriate when celiac disease is plausible [1]. In uncomplicated asymptomatic patients with negative bidirectional endoscopy, an initial trial of iron supplementation is generally favored over routine immediate video capsule endoscopy [1].

7. Oral Iron Therapy

Oral iron remains appropriate first-line treatment for many clinically stable adults. Ferrous sulfate is commonly preferred because it is inexpensive and effective, although no oral formulation has a clear universal efficacy advantage [2]. Contemporary AGA best-practice advice recommends oral iron no more than once daily; every-other-day dosing may be better tolerated in some patients with similar or adequate absorption [2]. BSG guidance similarly recommends one tablet daily of ferrous sulfate, fumarate, or gluconate, with every-other-day dosing or parenteral iron when intolerance occurs [3].

A practical initial target is approximately 50–100 mg of elemental iron once daily, adjusted to the formulation and patient tolerance. Food can reduce absorption but may improve gastrointestinal tolerability. Common adverse effects include nausea, epigastric discomfort, constipation, diarrhea, metallic taste, and dark stools. The regimen should be simplified whenever possible to maximize adherence.

8. Monitoring Response and Treatment Failure

Hemoglobin should be reassessed after treatment initiation, commonly within 2–4 weeks. BSG recommends monitoring for a hemoglobin response during the first 4 weeks and continuing treatment for approximately 3 months after hemoglobin normalization to replenish marrow iron stores [3]. Duration should be individualized when blood loss, malabsorption, or chronic disease persists.

An inadequate response should trigger reassessment rather than indefinite continuation of the same regimen. Important causes include poor adherence, persistent gastrointestinal or gynecological blood loss, malabsorption, incorrect diagnosis, chronic inflammation, CKD, mixed vitamin B12 or folate deficiency, and insufficient treatment duration.

9. Intravenous Iron

Intravenous (IV) iron should be considered when oral iron is not tolerated, iron stores fail to improve with an adequate oral trial, oral absorption is unlikely to be effective, clinically important malabsorption exists, ongoing losses exceed oral replacement, or rapid repletion is required [2]. IV iron is also commonly used in CKD and selected patients with active inflammatory bowel disease or after bariatric surgery.

Modern preparations permit larger iron replacement doses with relatively few treatment sessions. Selection should consider total iron deficit, product labeling, infusion capacity, cost, patient preference, kidney function, and formulation-specific adverse effects. Iron sucrose has extensive experience, particularly in CKD, but usually requires multiple smaller administrations. Ferric carboxymaltose allows larger single-session doses but is associated with a clinically important risk of hypophosphatemia. Randomized trials have shown substantially higher rates of hypophosphatemia with ferric carboxymaltose than with ferric derisomaltose [6]. Serum phosphate assessment is reasonable in patients receiving repeated ferric carboxymaltose or those at increased risk.

10. Iron Deficiency in Chronic Kidney Disease

Anemia in CKD is multifactorial and may reflect relative erythropoietin deficiency, systemic iron deficiency, iron-restricted erythropoiesis, inflammation, blood loss, and shortened red-cell survival. KDIGO 2026 uses the terms systemic iron deficiency and iron-restricted erythropoiesis in place of the older absolute and functional iron deficiency terminology [7]. Ferritin and TSAT remain the principal practical tests despite recognized limitations.

For adults with anemia and CKD G5 receiving hemodialysis, KDIGO 2026 suggests initiating iron when ferritin is ≤500 ng/mL and TSAT is ≤30%, with IV iron preferred in hemodialysis [7]. For adults with anemia and CKD not receiving hemodialysis, iron may be initiated when ferritin is <100 ng/mL with TSAT <40%, or ferritin is 100–300 ng/mL with TSAT <25% [7]. In non-hemodialysis CKD, oral or IV iron can be selected according to patient preferences, severity, tolerability, efficacy, availability, and cost. KDIGO considers it reasonable to withhold routine iron when ferritin is >700 ng/mL or TSAT is ≥40%, and to suspend iron during active systemic infection [7].

11. Special Clinical Situations

In active inflammatory bowel disease, intestinal inflammation may impair absorption and worsen oral iron intolerance; IV iron is often appropriate when deficiency is substantial or oral therapy fails. After bariatric surgery involving the duodenum, IV iron should be considered when oral supplementation does not restore iron stores [2]. In older adults, IDA warrants careful evaluation for occult gastrointestinal disease and should not be attributed to age alone.

Iron deficiency in heart failure deserves separate disease-specific consideration because diagnostic thresholds and evidence for IV iron differ from conventional IDA. Similarly, pregnancy requires pregnancy-specific diagnostic and therapeutic thresholds and is beyond the principal scope of this adult general-medicine review.

12. Practical Clinical Approach

A practical sequence is: (1) confirm anemia and assess ferritin; (2) add TSAT and inflammatory markers when ferritin is equivocal or chronic disease is present; (3) investigate the cause, with particular attention to menstrual and gastrointestinal blood loss, celiac disease, malabsorption, medication exposure, and CKD; (4) begin oral iron in stable patients when appropriate; (5) reassess hemoglobin in approximately 2–4 weeks; and (6) if response is inadequate, evaluate adherence, ongoing loss, malabsorption, inflammation, CKD, and alternative diagnoses before switching to or adding IV iron.

13. Common Clinical Pitfalls

Common errors include excluding iron deficiency because MCV is normal; excluding iron deficiency because ferritin is normal in a patient with inflammation; treating IDA without investigating the cause; prescribing multiple daily oral doses that worsen intolerance; continuing ineffective oral therapy indefinitely; and assuming that all anemia in CKD is due solely to erythropoietin deficiency.

14. CONCLUSIONS

Iron deficiency anemia is common and treatable, but optimal management requires more than normalization of hemoglobin. Ferritin remains central to diagnosis, while TSAT and the clinical context are especially important in inflammation and CKD. Current evidence supports simpler oral iron schedules, generally no more than once daily, with alternate-day treatment as a useful option for selected patients. IV iron is effective when oral therapy is unsuccessful, poorly tolerated, inadequately absorbed, or clinically insufficient.

Most importantly, unexplained IDA should not be managed by iron replacement alone. Appropriate investigation for chronic blood loss, gastrointestinal disease, gynecological pathology, malabsorption, CKD,

and other underlying disorders remains essential to safe adult care.

Table 1: Practical Interpretation of Iron Studies

Ferritin	TSAT	Practical interpretation
Low	Low	Systemic/absolute iron deficiency strongly supported
Normal or high	Low	Consider iron-restricted erythropoiesis, inflammation, or CKD
Low	Normal	Possible early deficiency or laboratory variation; reassess context
Normal or high	Normal	Major systemic iron deficiency less likely; consider alternative causes

Table 2: Common Oral Iron Preparations

Preparation	Typical tablet strength	Approximate elemental iron*
Ferrous sulfate	200–325 mg	~60–65 mg
Ferrous fumarate	200 mg	~65 mg
Ferrous gluconate	300–325 mg	~35–38 mg

*Exact elemental iron content varies by product and country; verify the product label.

Table 3: Causes of Inadequate Response to Oral Iron

Cause	Clinical action
Poor adherence	Review dosing, adverse effects, and barriers
Persistent blood loss	Reassess gastrointestinal and gynecological sources
Malabsorption	Consider celiac disease, bariatric surgery, IBD, gastric pathology
Incorrect or mixed diagnosis	Review smear, B12/folate, hemoglobinopathy, marrow disease
CKD/inflammation	Interpret ferritin with TSAT; apply disease-specific guidance
Insufficient duration/dose	Confirm elemental iron exposure and timing of reassessment

Table 4: Practical Comparison of Selected Intravenous Iron Preparations

Feature	Iron sucrose	Ferric carboxymaltose	Ferric derisomaltose
Dose strategy	Multiple smaller doses	Larger doses; often fewer visits	Large single-dose replacement possible
CKD experience	Extensive	Established	Established
Hypophosphatemia	Lower recognized risk	Higher recognized risk	Lower than ferric carboxymaltose in head-to-head trials
Practical advantage	Long experience	Rapid repletion with fewer visits	Rapid repletion with lower hypophosphatemia risk than FCM

Figure 1: Proposed Clinical Algorithm

- Adult with anemia → CBC + ferritin
- If uncertainty/chronic disease → add TSAT ± CRP
- Confirm iron deficiency → identify cause (GI, gynecologic, malabsorption, diet, CKD)
- Stable and oral absorption expected → oral iron once daily; consider alternate-day if intolerance
- Oral therapy unsuitable/ineffective or rapid repletion needed → intravenous iron
- Reassess hemoglobin in ~2–4 weeks
- Inadequate response → reassess adherence, ongoing blood loss, malabsorption, inflammation, CKD, and alternative diagnoses

Author Contributions

Conceptualization, M.M.R. and M.F.W.; literature review, M.M.R. and M.F.W.; writing—original draft preparation, M.M.R. and M.F.W.; writing—review and editing, M.M.R. and M.F.W. All authors have read and agreed to the submitted version of the manuscript.

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Conflicts of Interest

The author(s) declare no conflict of interest.

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