Clinical Guidance: Best Practices in the Management of Iron Deficiency and Iron Deficiency Anemia

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Do	• **Screen** for iron deficiency (ID) and iron deficiency anemia (IDA) in patients at risk, especially in people who menstruate, are pregnant, or lactating.[1–4] • **Diagnose** patients with ferritin <30 mcg/L (adults) or <20 mcg/L (pediatric) with ID/A and offer iron therapy.[4–6] • **Investigate** and manage underlying causes of ID/A (e.g., comorbid conditions, increased loss).[5,7,8] • **Treat** with intravenous (IV) iron when oral iron is not tolerated or ineffective after 4-12 weeks.[1–4,9,10] • **Assess** all patients for hematologic treatment response following iron therapy.[10] • **Monitor** patients for IV adverse events per product monograph. • **Refer** to your institution's clinical decision support guidelines specific to iron deficiency.
Stop	• If not responding to oral iron supplementation, **stop oral** and assess eligibility for IV iron.[11]
Consider	• Increasing dietary iron alone is **not sufficient** to treat ID/A.[7,10] • Most people with ID/A have **normal red blood cell** mean corpuscular volume.[1,3,4,9,10] • Iron deficiency without anemia **may require treatment**.[1,3,4,9,10] • IV iron has a **favourable risk/benefit profile**, with efficacy, benefits, and safety profile often outweighing the risk of severe adverse events, such as anaphylaxis in 1:200,000.[10,12,13]

Background

Globally, iron deficiency is the most prevalent micronutrient insufficiency that negatively impacts health, quality of life, and functioning.[14] Iron deficiency is characterized by inadequate iron stores or availability, leading to compromised red blood cell production and decreased hemoglobin concentration.[1,2]

Iron deficiency can occur without anemia (ID), but prolonged, untreated deficiency may progress to iron deficiency anemia (IDA). IDA is the most common cause of anemia, affecting more than 1.2 billion individuals.[1,2] In Canada, iron deficiency is found in 7% of Canadians overall, ~20% of women aged 14-50 years, 30% of pregnant individuals, and many are unaware that they are iron deficient.[1–3,15,16]

Symptoms of ID/A[1,3,4,9,10,17]

Symptoms of ID/A are related to decreased oxygen delivery to the entire body and can seriously impact quality of life, although many patients have no symptoms.[1] A diagnosis may be missed because the common symptoms of ID/A can often be overlooked as pressures of daily life.

ID Symptoms
- Physical fatigue
- Cognitive (e.g., mood changes, impaired memory, headache)
- Decreased exercise tolerance
- Restless leg syndrome, pica

IDA Symptoms
- ***ID symptoms +***
- Shortness of breath
- Neurological (e.g., insomnia, lightheaded, fainting)
- Cardiac (e.g., rapid heart rate, palpitations, chest pain/tightness)
- Muscle weakness
- Pale skin, cold hands/feet
- Brittle nails/hair

Who is at risk of ID/A?[4,5,9,18-21]

Screening should occur in patient populations with risk factors for ID/A, including those with:

- **Higher iron demands:** menstruating, pregnant, lactating people; children/adolescents undergoing rapid growth
- **Comorbid conditions:** gastrointestinal disorders/surgery, chronic kidney disease, chronic intravascular hemolysis
- **Decreased availability:** conditions that cause chronic inflammation or affect nutrient absorption, active celiac disease, dietary restrictions, large consumption of cow's milk, *H. pylori*, post-bariatric surgery
- **Increased loss:** heavy menstrual periods, chronic gastrointestinal blood loss
- **Social determinants of health:** lower socioeconomic status, minority race or ethnicity

Impacts of iron deficiency

Iron deficiency is associated with:[9,14]
- Decreased health-related quality of life
- Impairment in cognitive performance in young children
- Adverse outcomes in pregnancy for both mothers and newborns
- Decreased physical capacity in adults
- Cognitive decline in the elderly

Iron deficiency definitions[11]

- **Iron deficiency:** insufficient iron stores to meet the body's needs
- **Iron deficiency with anemia:** ID with reduced erythropoiesis, may be severe despite normal hemoglobin
- **Absolute iron deficiency:** reduced iron intake, defective absorption, chronic blood loss, or increased need
- **Functional iron deficiency:** sufficient iron stores that aren't being used well, often with inflammatory states (e.g., chronic kidney disease, malignancy)
- **Anemia in pregnancy:** hemoglobin levels in 1st and 3rd trimester <110 g/L, 2nd trimester <105 g/L[12,19–21]

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How to make the diagnosis of ID/A

ID/A diagnosis involves careful history taking and physical examination, which are essential in identifying risk factors and possible etiology, guiding laboratory testing, and identifying the underlying cause of the iron deficiency.[4]

Investigations

While there is no current consensus on diagnostic cutoff levels for ID/A, serum ferritin is recommended. Several factors, such as inflammation and age, can impact ferritin concentrations. If a false-normal ferritin is suspected, combining different biomarkers may assist in making the diagnosis. CBC alone is an inadequate screen for ID/A, as the sensitivity and specificity of low hemoglobin and microcytosis are limited.[4,10,20,22]

Initial workup should include:	Adult (⩾18)	Pediatric (<18)	Interpretation of results[5,6]
Serum ferritin	<30 mcg/L	<20 mcg/L	Result consistent with ID
	30–50 mcg/L	20–50 mcg/L	Probable ID*
	51–100 mcg/L		Possible ID if risk factors are present*
	101–300 mcg/L		ID unlikely*
	⩾600 mcg/L		Consider test for iron overload
Complete blood count (hemoglobin)	Normal		No anemia, interpret alongside ferritin level to assess if ID
	Low		Anemia, interpret alongside ferritin level to assess if IDA
In patients with concomitant inflammation (e.g. CKD) AND ferritin ⩾30 mcg/L (adults) or ⩾20 mcg/L (pediatric), add:[5,6]			
Fasting serum iron	Low		Possible ID
Total iron binding capacity	High		Possible ID
Transferrin saturation	<20%		Result consistent with ID

**in the absence of concomitant inflammation*

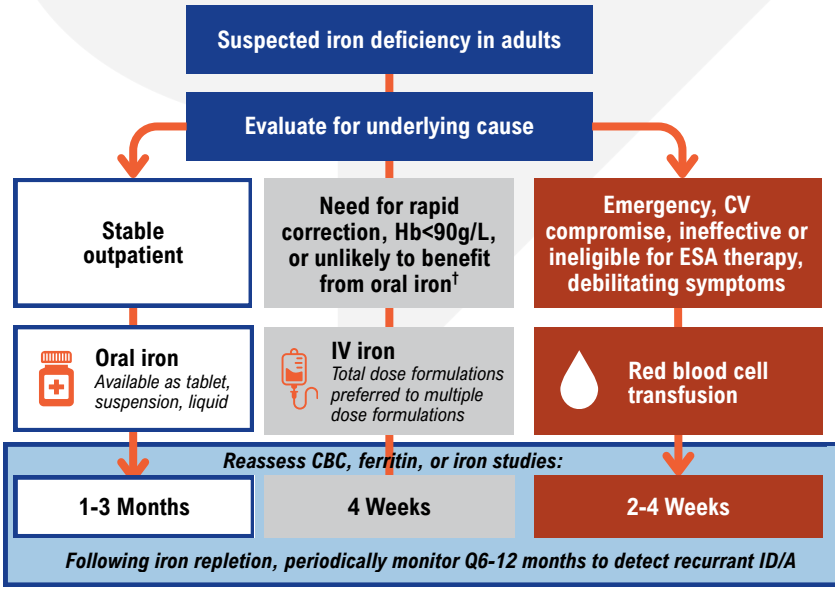
Management of ID/A[2,7,10,23–31]

Studies show improvement in energy levels, cardiovascular health, cognition, energy, and health-related quality of life with iron therapy (oral, IV, or transfusion). While consuming enough iron through food is an important part of preventing iron deficit, people with ID/A need more iron than can be consumed through diet alone. Hemoglobin target level and iron stores may vary in different patient groups and between patients. Iron therapy decisions should consider patient preferences, resource availability, insurance coverage, treatment costs, and healthcare resources. Most cases of ID/A can be managed in primary care, however, referral to a specialist may be necessary in patients who are refractory to iron therapy, complex cases, or have an unexplained etiology following investigations.[32]

Algorithm for management decisions for adults with ID/A

Optimizing oral iron

- Educate patients on adherence and managing side effects
- Offer once-daily oral iron, or alternate-day dosing if not well tolerated
- Take on an empty stomach/ with an acidic drink
- After taking, avoid milk, tea, coffee, calcium pills, antacids, proton pump inhibitors, H2-receptor blockers, thyroid medications, and some antibiotics for 2 hours
- Dark stool is normal and expected
- Manage potential GI adverse effects by adding fibre, fluids, and daily polyethylene glycol; or changing formulation
- Eat foods high in iron and vitamin C



†Unlikely to benefit from oral iron

- Gastric bypass surgery
- Intestinal resection or short bowel syndrome
- Celiac disease, inflammatory bowel disease
- Gastritis or ulcers
- Certain gastrointestinal tract cancers
- Inflammatory disorders (e.g., autoimmune or chronic infection)
- Iron loss is greater than the body's ability to absorb iron

Assessing treatment response using Hb

Adequate: Increased by >20 g/L
Inadequate: Increased by <20 g/L
Failure: No improvement or worsening of Hb
If insufficient response or inability to adhere to treatment, trial a different formulation or escalate to next treatment level

Adapted from Benson AE, et al. Lancet Haematol. 2025;12(5):e376-e388.

CV = cardiovascular, ESA = erythropoeitin stimulating agents; GI = gastrointestinal Hb = hemoglobin

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Management of ID/A with oral or IV iron

Management	Oral Iron[10,22,23,33–37]	IV Iron[1,10,22,38–42]
Agents, common doses, and administration times	• Ferrous fumarate (Palafer®), 300 mg daily[33] • Ferrous gluconate (Fergon®), 300 mg daily • Ferrous sulfate (Fer-In-Sol®, Feosol®), 300 mg daily • Polysaccharide iron complex (FeraMAX®, Triferexx®, Polyride Fe®), 150 mg daily • Liposomal iron (Ferosom®), 30 mg daily • Heme iron polypeptide (Proferrin® ES, OptiFer® Alpha), 11 mg, 1–3 times a day; or (Hemaforte® heme iron), 35 mg daily[34] • Ferric maltol (ACCRUFeR®), 30 mg twice a day[36]	IV iron dosing and schedule must be individually established for each patient as per each product monograph, based on indication and either fixed dosing (fe-derisomaltose only) or iron deficit: • Determination of "iron deficit" (total dose needed) using hemoglobin deficit equation (Hb and body weight) • Divide iron deficit into appropriate individual doses • Administer until total dose complete **Multiple dose formulations (⩾3 administrations)** • Sodium ferric gluconate complex in sucrose (Ferrlecit®): 125 mg, 60 min., every other day for 8 sessions • Iron sucrose (Venofer®): 100 mg, 2–180 min., weekly for 3-5 weeks **Total dose formulations (1-2 administrations)** • Ferric derisomaltose (Monoferric®): 20 mg/kg, at least 20–30 min., single infusion, max 1500 mg per single dose • Ferric carboxymaltose (Ferinject®): 15 mg/kg, at least 3–15 min., single infusion or weekly for 2 weeks, max 1000 mg per single dose
Populations	• Pediatric, adult, geriatric, pregnancy use	• Adult patients ⩾18 years • Refer to product monographs for special populations (e.g. pediatric, geriatric, chronic kidney disease, heart failure)
Contraindications	• Patients with iron-overloaded states such as hereditary hemochromatosis, hemosiderosis, or have a history of hemolytic anemia	• Evidence of iron overload, known hypersensitivity, anemia not caused by iron deficiency • Fe-gluconate: severe inflammatory diseases of the liver/kidneys • Fe-derisomaltose: decompensated liver cirrhosis or active hepatitis
Potential adverse events	• Side effects are common and dose dependent, including nausea, constipation, bloating, diarrhea, metallic taste, or dark stool	• Infusion reactions, including isolated skin, respiratory, or gastrointestinal symptoms • Hypersensitivity reactions can be mild (such as Fishbane), and rarely, severe (such as anaphylaxis)
Monitoring	• Monitor ferritin levels to assess hematologic response after 1-3 months • Following iron repletion, periodically monitor ferritin Q6-12 months to detect any recurrent ID/A	• Monitor ferritin levels, transferrin saturation, and serum iron to assess hematologic response or overload, no sooner than 4 weeks post-infusion • In patients at high risk for hypophosphatemia, monitor serum phosphate levels for chronic low serum phosphate prior to repeated doses, which can lead to osteomalacia, particularly with fe-carboxymaltose • Following iron repletion, periodically monitor ferritin Q6-12 months to detect any recurrent ID/A
Practical considerations	• **Benefits:** Over-the-counter availability and cost effective • **Drawbacks:** Adherence can be poor, in part due to high rates of adverse effects, and variable absorption rates	• **Benefits**: Optimizes hemoglobin levels quickly in stable outpatients, benefits those intolerant or not responding to oral iron, increased efficacy, improved adherence, decreased discontinuation rate, and acceptable safety profile compared to oral iron • **Drawbacks**: Requires visit to infusion centre or hospital for administration, high or repeated doses may lead to prolonged hypophosphatemia/osteomalacia, particularly with fe-carboxymaltose

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For additional resources on ID/A, please visit:

https://www.canadiankt.org/nurse-training-iv-iron
https://www.hemequity.com/our-resources-for-healthcare-providers
https://www.hemequity.com/our-resources-for-patients
https://www.hemequity.com/toronto-iv-iron-policy
https://gynqi.com/intravenous-iron-infusions/

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