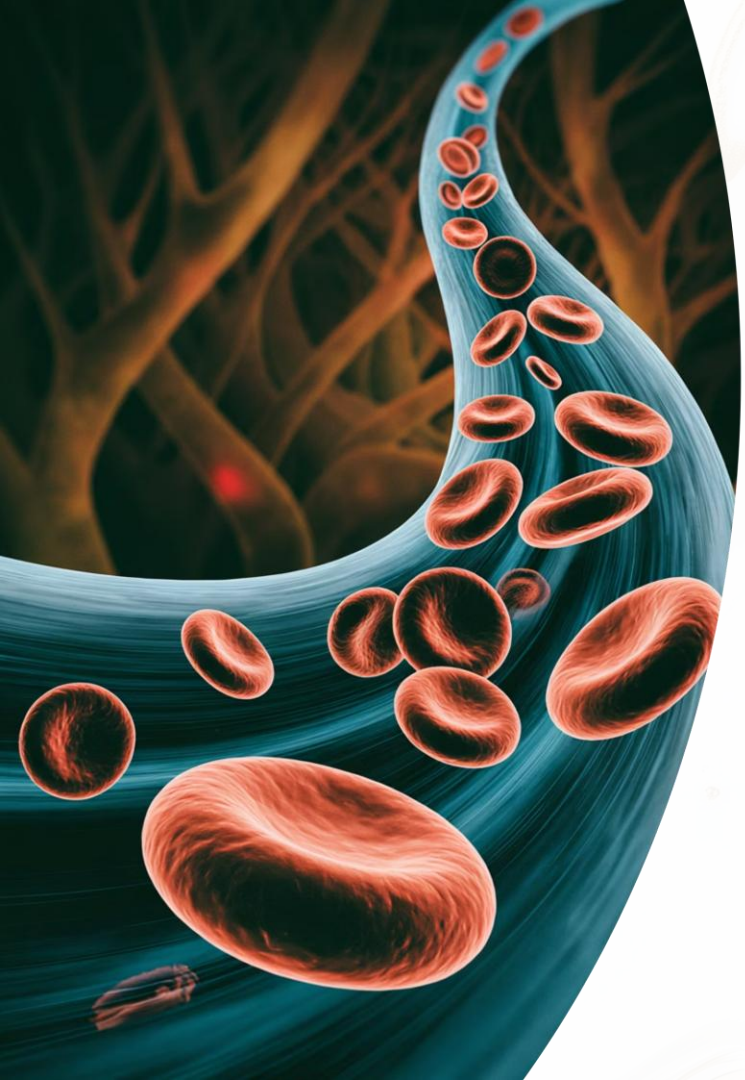

Iron Deficiency & Iron Deficiency Anemia

A clinical deep-dive into physiology, diagnostic evaluation, and evidence-based management — aligned with Canadian Hematology Society and Canadian Association of Gastroenterology guidelines.

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Disclaimer:

- I do not have any affiliation with any association, organization or entity on presenting this lecture
- I am not receiving any monatery compensation or incentives upon sharing the following information
- No conflict of interest

Objectives:

- Define Iron Deficiency vs Iron Deficiency Anemia
- Understand Iron Metabolism and Its Faith In The Body
- Learn Causes of Iron Deficiency
- Identifying Lab Work Up in Diagnosing Iron Deficiency
- Learn about Treatment Options

Iron Deficiency vs Iron Deficiency Anemia

Iron deficiency anemia (IDA) is a form of anemia that caused by inadequate iron stores (Ferritin) or availability leading to compromised RBC production and Hb concentration .

An Iron deficient patient however does not necessarily have an IDA.

POP QUIZ

- Which organ stores the highest amount of iron in the body?

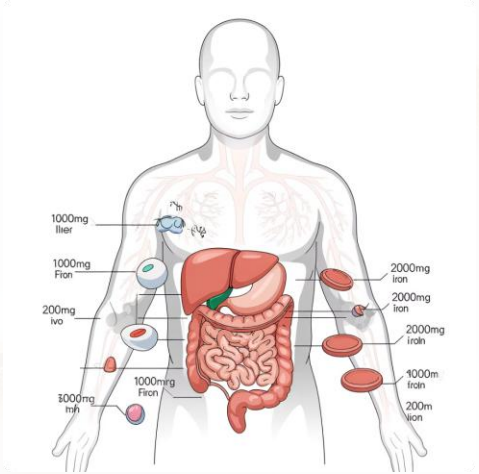
Systemic Iron Homeostasis

Physiology of Iron Absorption

Iron physiology is a tightly regulated, body-wide recycling system. Dietary Iron is absorbed through enterocytes in Duodenum in the form of heme iron (Fe^{2+}, ~25% absorbed) and non-heme iron (Fe^{3+}, ~5–10% absorbed). Iron is carried in the blood by transferrin, delivered to the organs as a substrate for storage or utilization. For example, iron is transferred to bone marrow for erythropoiesis, and continuously recovered from aging red blood cells by the spleen. Excess iron is stored in the liver and other tissues, while hepcidin serves as the master regulator by limiting intestinal absorption and iron release when body iron stores are sufficient.

Major Iron Compartments

- **RBC / Hemoglobin (~2000 mg):** Primary functional iron pool for oxygen transport.
- **Liver (~1000mg):** Major storage site and source of regulated iron release
- **Spleen (~600 mg):** Recycles iron from senescent red blood cells.
- **Bone marrow (~300mg):** Uses iron to support hemoglobin synthesis and new RBC production.
- **Other tissues (Macrophages, Skeletal Muscle, Heart and Brain ~350-600mg)**



Hepcidin rises with iron repletion and inflammation, and falls when iron demand increases.

Total body Iron ~3.5g with daily loss of Iron ~1-2mg from enterocytes shedding and GU bleeding while replenishing ~1-2mg via Diet and GI absorption.

Iron Metabolism

Intracellular Transport & Systemic Regulation

Enterocyte Uptake

DMT-1 imports dietary Fe2+ into enterocytes

Plasma Loading

Hephaestin oxidizes Fe2+; transferrin binds Fe3+

Intracellular Fate

Stored in ferritin or routed to ferroportin

Hepcidin Control

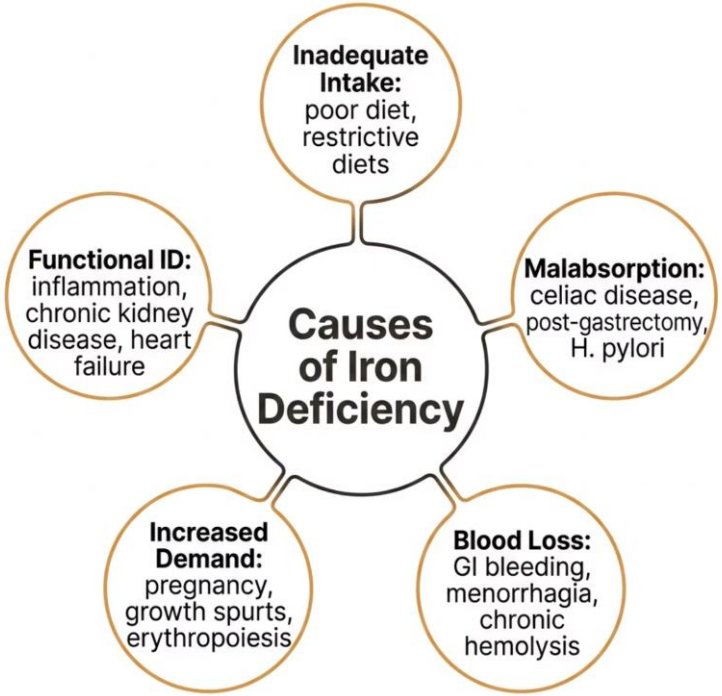
High iron/inflammation increases hepcidin, blocks ferroportin

Hepcidin — the master iron hormone synthesized by the liver — binds and degrades ferroportin, the sole known iron export channel. In iron deficiency, hepcidin is suppressed, maximizing duodenal absorption and macrophage iron release.

Divalent Metal transporter-1 (DMT-1) is responbsile for allowing Ferritin into the cell while ferroportin is responsible for iron into the blood.

Etiology & Red Flags

Finding the Underlying Cause



When to Investigate Further

Per **CAG guidelines**, all males and post-menopausal females with confirmed IDA require bidirectional endoscopy to exclude GI malignancy or inflammatory bowel disease.

⚠ Red flag symptoms — melena, hematochezia, weight loss, dysphagia — mandate urgent upper and lower endoscopy regardless of age.

Celiac serology (anti-tTG IgA with total IgA) should be ordered in all patients with unexplained IDA or persistent non-response to oral iron.

Clinical Consequences of Iron Deficiency

Hematological Manifestations

Anemia

Individuals at elevated risk for ID:
- Children aged 6m-5yoa
- women of childbearing age
- pregnant woman
- others (vegetarians, freq blood donors)

Non-Hematological Manifestations

- Cognitive impairment, decrease memory, learning and concentration
- Impaired immune function
- developmental delays in children
- Adverse pregnancy outcomes for mother and baby, Maternal IDA, risk for preterm baby, low birth weight
- restless leg syndrome
- dizziness, cold extremities, brittle mails
- hair loss and recurrent headaches, Chelitis, atrophic glossitis

In patients with HF and ID:

- reduced energy
- reduced exercises capacity
- fatigue
- impaired quality of life and poor prognosis

Diagnostic Work-Up

A structured, tiered laboratory approach is essential to differentiate true iron deficiency from anemia of chronic disease and to quantify severity.

Pop Quiz!

What lab test is the gold standard to differentiate between anemia of chronic disease vs iron deficiency?

Laboratory Investigations

Key Tests & Their Clinical Significance

Test	Threshold	Clinical Significance
Serum Ferritin	<30 µg/L (ID); <15 µg/L (IDA) *	Best single marker of iron stores; acute-phase reactant — interpret with CRP
Serum Iron	<10.7 µmol/L	Fluctuates with diet/diurnal rhythm; use in context of TIBC
TIBC / Transferrin	TIBC >72 µmol/L	Rises in ID; transferrin saturation <16% indicates functional iron deficiency
Transferrin Saturation	<16%	Reflects iron available for erythropoiesis; key for IDA vs ACD distinction
CBC + RBC Indices	MCV <80 fL, MCH <27 pg	Microcytic hypochromic pattern; low Hgb confirms anemia stage
Reticulocyte Hgb (CHr)	<28 pg	Early functional iron deficiency marker; responds within 72 hrs of treatment
Soluble Transferrin Receptor	>28.1 nmol/L	Elevated in ID even with inflammation; sTfR:log ferritin ratio >2 suggests ID
CRP / ESR	Elevated	Detects inflammation that falsely elevates ferritin; adjust ferritin threshold to <100 µg/L if CRP elevated

Assessment

General Principles:

- Bidirectional Endoscopic investigations in post menopausal and men with ID or IDA
- Premenopausal female with suggestive/concerning symptoms
- Confirm whether there is a history of significant over non GI blood loss
- All patients should be screened for celiac dz (Anti-tTG ab and IgA lvls) (sometimes serum electrophoresis)
- Small intestine evaluation is not routinely performed unless there is suggestion of symptoms or a question of small intestinal disease and the anemia is not corrected with iron supplement
- **Fecal blood testing (FOBT, FIT) is not of benefit !!!**

Clinical Management

Oral Iron Therapy: First-Line Treatment

Recommended Regimens

Ferrous Sulfate 300 mg

Contains ~60 mg elemental iron per tablet. **150–200 mg elemental iron/day** is the standard target. Administer on an empty stomach for maximal absorption.

Alternate-Day Dosing

Canadian Hematology Society recommends **every-other-day dosing** (e.g., 150 mg elemental iron q48h) to exploit the post-absorption hepcidin nadir and improve net uptake vs. daily dosing.

Adjuncts to Enhance Absorption

Co-administer with **250 mg Vitamin C** to maintain luminal Fe^{2+} state. Avoid concomitant calcium, antacids, PPI, or tetracyclines within 2 hours.

Alternative Oral Formulations

For patients intolerant of ferrous sulfate (GI side effects in ~30%):

- **Ferrous gluconate 300 mg** (35 mg elemental iron) — better GI tolerability
- **Ferrous fumarate 300 mg** (99 mg elemental iron) — intermediate tolerability
- **Polysaccharide-iron complex** — lower GI burden, useful in IBD patients

Monitor CBC and ferritin at **4–8 weeks**. Target Hgb rise of ≥10 g/L at 4 weeks confirms adequate response. Continue therapy **3 months after Hgb normalization** to replete stores.

Oral Iron Options

Drug Class	Examples	Dose per tablet (mg)	Elemental iron content per tablet (mg)
Iron salts (taken on empty stomach/acidic environment)	Ferrous gluconate	240 325	27 38
	Ferrous sulfate	325	65
	Ferrous fumarate	325	106
Heme iron polypeptide	Proferrin®	398	11
Polysaccharide iron complex	Feramax*	150	150
Ferric citrate	Auryxia®	210	210
Ferrous bisglycinate	Easy Iron *	18.5-60	18.5-60

Note that there are MANY MANY options for oral iron!!!

*Oral iron is dosed once a day at most. Every-other-day iron dosing may be better tolerated for some patients with similar or equal rates of iron absorption as daily dosing.

McLoughery, TG et al. AGA Clinical Practice Update on Management of Iron Deficiency Anemia: Expert Review. 2024. 22 (8):p1575-1888.

Oral Iron Options

Many options available with different dosages.

e.g. Ferrous gluconate/fumerate, polysaccharide iron complex and ferrous bisglycinate are more common options.

Intravenous Iron Therapy

When to Escalate to IV Iron

Indications

- Oral iron intolerance or failure after 4–8 weeks
- Malabsorption (celiac, post-bariatric, IBD)
- Severe IDA (Hgb <80 g/L) requiring rapid repletion
- Concurrent ESA therapy (CKD, chemotherapy)

IV Formulations & Dosing

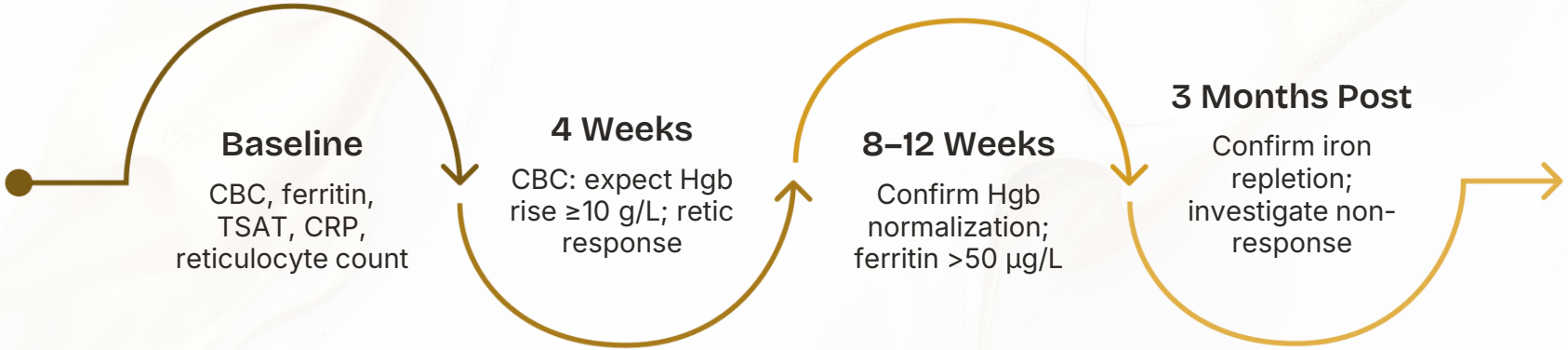
- **Ferric carboxymaltose (Ferinject®)**: up to 1000 mg over 15 min; single infusion preferred
- **Iron sucrose (Venofer®)**: 200–300 mg per session, multiple sessions required
- **Low molecular weight iron dextran**: total dose infusion possible; requires test dose

Total Dose Calculation

Use **Ganzoni formula**:
Total Iron Deficit (mg) = Weight (kg) × (Target Hgb − Actual Hgb) × 0.24 + 500 mg stores

Monitoring & Response Assessment

Treatment Response & Follow-Up Protocol



Response Targets

- Hgb rise ≥10 g/L within 4 weeks of oral iron
- Ferritin >50 µg/L at end of repletion
- TSAT >20% post-IV iron

Non-Response: Next Steps

- Confirm adherence and absorption
- Reassess for ongoing blood loss
- Review celiac serology, H. pylori status
- Consider hematology or GI referral

Summary & Key References

Clinical Takeaways

01

Diagnose Systematically

Use ferritin <20&30&50, TSAT, sTfR, and CBC together. Adjust ferritin threshold to <100 µg/L in inflammatory states (CRP elevated).

02

Identify the Cause

All males and post-menopausal women with IDA require bidirectional endoscopy. Order celiac serology in unexplained cases.

03

Optimize Oral Iron First

Prefer alternate-day dosing (150–200 mg elemental iron q48h) with Vitamin C. Continue 3 months post-Hgb normalization.

04

Escalate to IV When Indicated

Ferric carboxymaltose 1000 mg single infusion is preferred for rapid, high-dose repletion in malabsorption or severe IDA.

Key References: Canadian Hematology Society — Management of Iron Deficiency Anemia (2021) · Canadian Association of Gastroenterology — Iron Deficiency in IBD and GI Bleeding (2019) · Camaschella C. Iron-deficiency anemia. *NEJM* 2015;372:1832–1843 · Stoffel NU et al. Alternate-day oral iron supplementation. *Lancet Haematol* 2017;4:e524–e533

Thank you for your attention