Iron Deficiency Anemia

Iron deficiency occurs when the intake and absorption of iron are insufficient to replenish the body's loss.

Iron metabolism

Iron has a important role in many metabolic processes, and the average adult contains 3–5 g of iron, of which two-thirds is in the oxygen- carrying molecule haemoglobin.

A normal Western diet provides about 15 mg of iron daily, of which 5–10% is absorbed (~1 mg), principally in the duodenum and upper jejunum, where the acidic conditions help the absorption of iron in the ferrous form. Absorption is helped by the presence of other reducing substances, such as hydrochloric acid and ascorbic acid. The body has the capacity to increase its iron absorption in the face of increased demand – for example, in pregnancy, lactation, growth spurts and iron deficiency.

Once absorbed from the bowel, iron is transported across the mucosal cell to the blood, where it is carried by the protein transferrin to developing red cells in the bone marrow. Iron stores comprise ferritin, a labile and readily accessible source of iron, and haemosiderin, an insoluble form found predominantly in macrophages. About 1 mg of iron a day is lost from the body in urine, faeces, sweat and cells shed from the skin and gastrointestinal tract. Menstrual losses of an additional 20 mg a month, and the increased requirements of pregnancy (500–1000 mg) contribute to the higher incidence of iron deficiency in women of reproductive age.

Risk factors for development of iron deficiency.

- **Age:** infants; adolescents; premenopausal women; old age
- **Gender:** increased risk in women
- **Reproduction:** pregnancy, breast feeding
- **Travel/country of origin:** parasites (e.g. hookworm, schistosoma)
- **Gastrointestinal pathology:** appetite or weight changes; bleeding from rectum/melaena; gastric or bowel surgery
- **Drug history:** especially aspirin and non-steroidal anti-inflammatories
- **Social history:** diet, especially vegetarianism, age of weaning of infants

Causes of iron-deficiency anaemia

1. Dietary deficiency/lack

- Milk fed infants because of low iron content in breast milk
- Elderly with improper diet and poor dentition
- Vegetarians (contains poorly absorbable inorganic iron)

2. Impaired absorption

- Total/partial gastrectomy impairs iron absorption by decreasing hydrochloric acid and transit time through the duodenum
- Intestinal steatorrhea (اسهال دهنی) and chronic diarrhea
- Specific items in the diet, like phytates of cereals, tannates, carbonates, oxalates, phosphates and drugs can impair iron absorption

3. Increased demand/requirement

- Growing infants, children and adolescents
- Pregnancy and lactation

4. Chronic blood loss

Due to bleeding from the

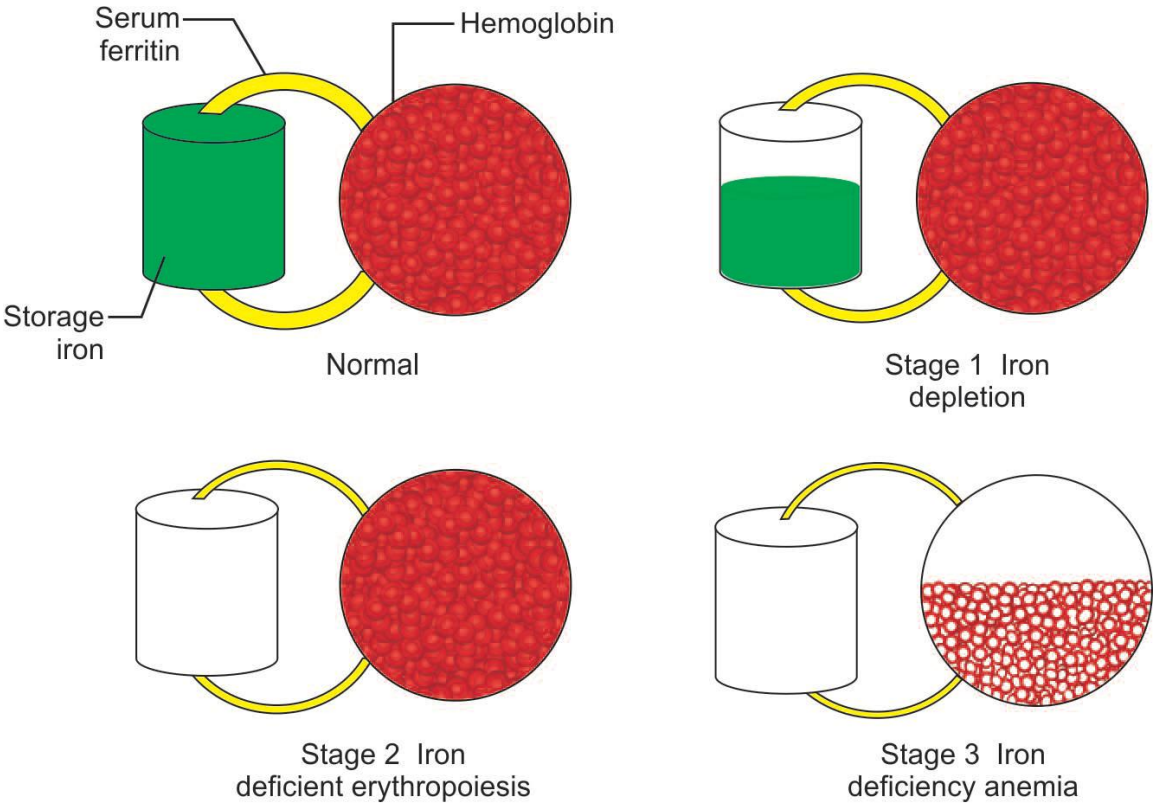
- Gastrointestinal tract (e.g. peptic ulcers, gastric carcinoma, colonic carcinoma, hemorrhoids, hookworm infestation or non-steroidal anti-inflammatory drugs)
- Urinary tract (e.g. renal or bladder tumors)
- Genital tract (e.g. menorrhagia, uterine cancer)
- Respiratory tract

Other

- Iatrogenic: multiple blood sampling (especially premature infants)

Table 1.1 Daily dietary iron requirements.

Male	1 mg
Adolescence	2–3 mg
Female (reproductive age)	2–3 mg
Pregnancy	3–4 mg
Infancy	1 mg
Maximum bioavailability from normal diet	~4 mg



Stage 1 (Iron depletion): In the initial phase, iron may be adequate to maintain normal levels of hemoglobin and **only serum ferritin** levels are **decreased.**

Stage 2 (Iron deficient erythropoiesis): Progressive depletion of iron reserves first lowers serum iron and transferrin saturation levels without producing anemia (Hb, MCV and MCH within normal range). Bone marrow, at this stage, shows iron deficient erythropoiesis.

Stage 3 (Iron deficiency anemia): Anemia only appears when depleted **iron stores** are accompanied by low serum iron, serum ferritin and transferrin saturation. As the serum iron level falls and transferrin saturation decreases below the critical value of <15%, the hemoglobin production is impaired. Morphologically, there is first reduction in the size (microcytic) and later increase in the central pallor (hypochromia) of red blood cells.

In **iron deficiency**, the failure of hemoglobin synthesis allows extra mitoses (cell division) to occur during erythropoiesis, with the production of small erythrocytes (microcyte).

When anemia is very severe, misshapen red blood cells (poikilocytes) are formed resulting in ineffective erythropoiesis. Many other iron proteins/enzymes like cytochrome c, cytochrome oxidase and myoglobin are reduced.

Clinical Features

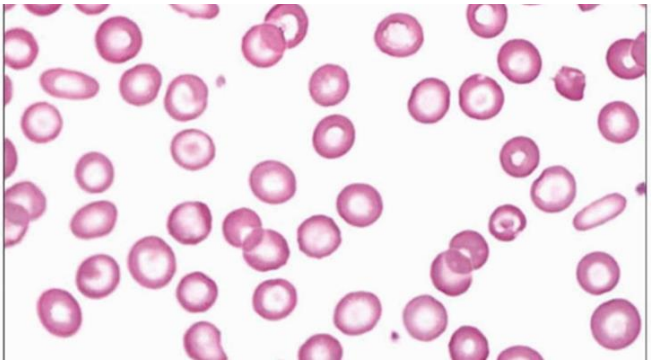
The clinical manifestations of the anemia are **nonspecific.**

- **Onset:** It is **insidious** and symptoms appear as anemia progresses. Patients become symptomatic as hemoglobin falls below 7 gm/dL.
- **Nonspecific symptoms:** Most of the patients complain of nonspecific symptoms like fatigue, palpitations, breathlessness, weakness and irritability.
- **Skins,** nail and other epithelial changes may be seen in chronic iron deficiency. Atrophy of the skin occurs in about a third of patients and nail changes such as koilonychia (spoon-shaped nails) may result in brittle, flattened nails
- **Pharyngeal/esophageal webs:** Folds (webs) of mucosa are formed at the junction of the hypopharynx with esophagus. These webs cause dysphagia (difficulty in swallowing) mainly to solid foods.

Laboratory investigations

Investigations in iron-deficiency anaemia.

- Full clinical history and physical examination
- Full blood count and blood film examination
- Haematinic assays (serum ferritin, vitamin B12 folate)
- Percentage hypochromic red cells and soluble transferrin receptor assay (if available)
- Urea and electrolytes, liver function tests



Tests Analysis

1- Hb ↓ **2-** MCV ↓ (<76fL) & MCHC ↓ **3-** RDW ↑ **4-** Serum ferritin ↓, Fe ↓ & TIBC ↑ **5-** sTfR ↑ **6-** % hypochromic RBCs &- Zinc protoporphyrin ↑ (ZPP)

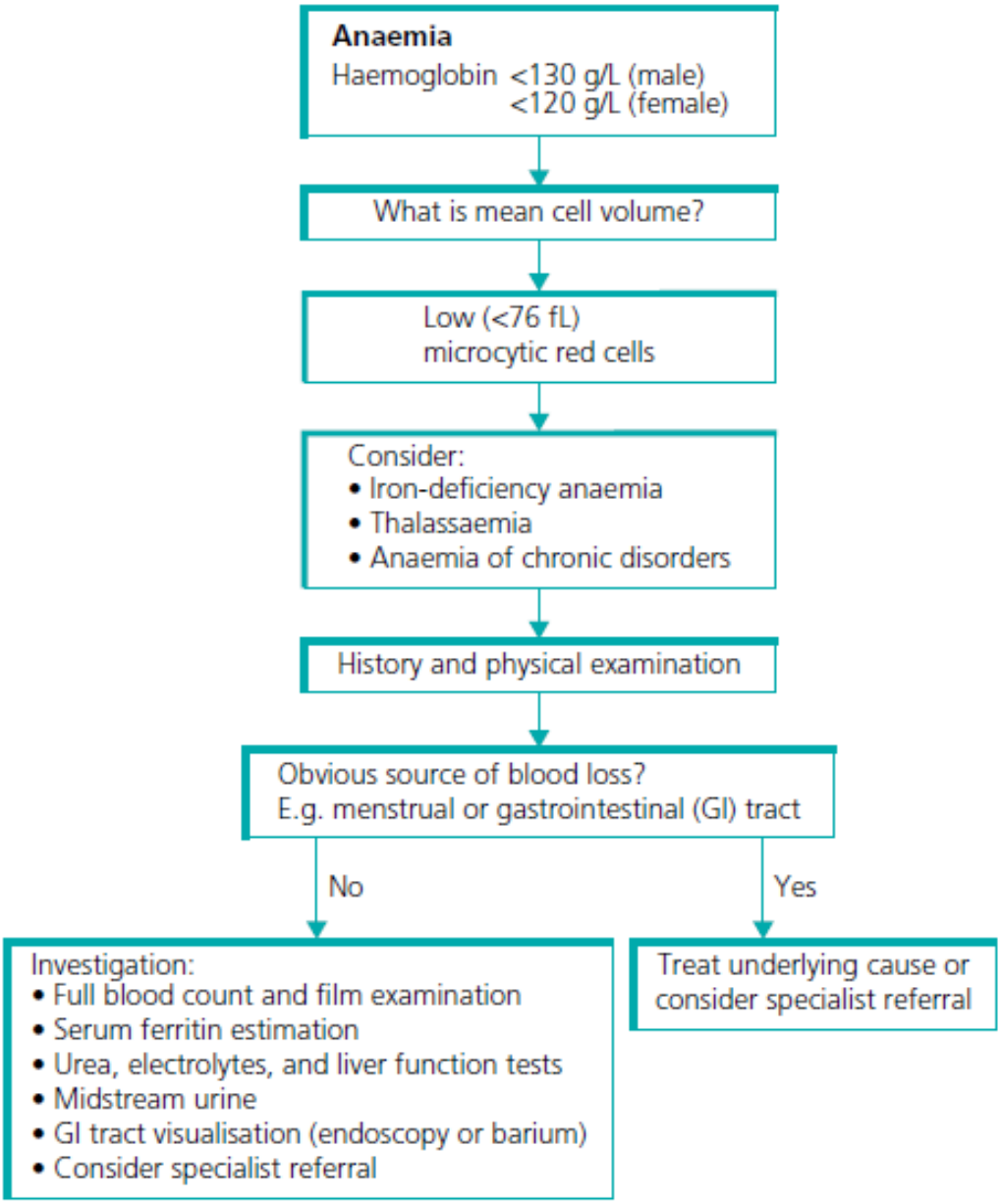


Figure 1.2 Diagnosis and investigation of iron-deficiency anaemia.

Iron dose calculation (Ganzoni formula).

Total dose (mg) = Body weight (kg) × [Target Hb - Actual Hb] (g/L) × 0.24 + 500 mg for iron stores

NOTE: Use 500 mg for adults and children ≥35 kg; use 15 mg/kg if <35 kg

[Where 0.24 is the percentage blood volume by weight (7%) × iron content of haemoglobin (Hb, 0.34%) × 1000 (grams to milligrams conversion): The factor 0.24= 0.0034 x 0.07 x 1,000].
* For example a 70 kg female with Hb 80 g/L has an iron deficit of:
= 70 x (150 – 80) x 0.24 + 500 = 1676 mg i.e. approx. 1700 mg

Table 1.4 Elemental iron content of various oral iron preparations.

Preparation	Amount (mg)	Ferrous iron (mg)
Ferrous sulphate	200	65
Ferrous gluconate	300	35
Ferrous fumarate	210	65–70

Failure to respond to oral iron therapy

Box 1.4 **Intravenous iron preparations.**

Compound	Trade name	Elemental iron concentration (mg/mL)	Administration
Iron hydroxide dextran	CosmoFer	50	Total dose infusion (max. 20 mg iron/kg body weight)
Iron isomaltoside	Monofer	100	Total dose infusion (max. 20 mg iron/kg body weight)
Iron sucrose	Venofer	20	Max. dose 200 mg iron, up to three times per week
Ferric carboxymaltose	Ferinject	50	Max. dose 1000 mg iron, once per week