Dr. Khaled Al-Qaoud

Chapter 3

Hypochromic Anemias

Production of Hb and causes of Iron deficiency anemia

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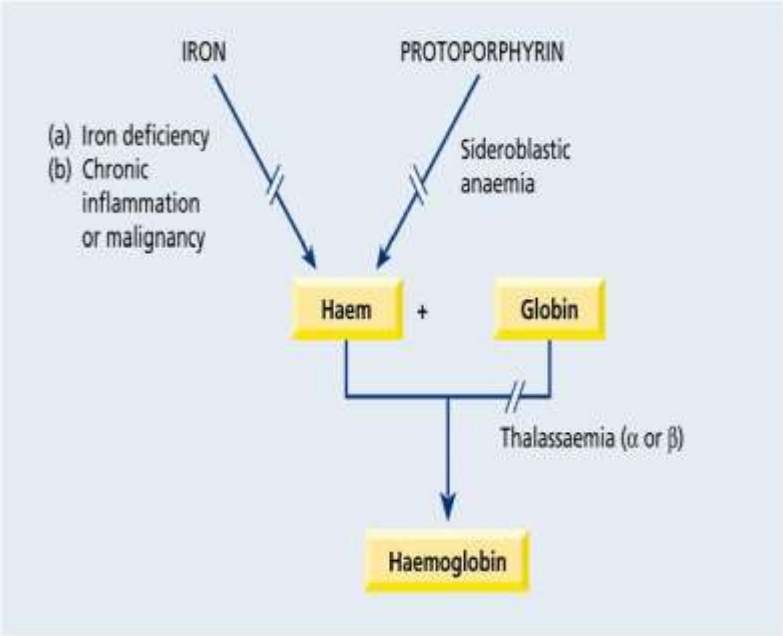

causes of Iron deficiency anemia

1. **Lack of iron**
2. **Defect of iron release from Macrophages**
3. **Failure of protoporphyrin synthesis**
4. **Failure of globin synthesis**
5. **Lead poisoning**

Reasons for Iron deficiency

- Blood Loss
  - Gastrointestinal Tract
  - Menstrual Blood Loss
  - Urinary Blood Loss (Rare)
  - Blood in Sputum (Rarer)
- Increased Iron Utilization
  - Pregnancy
  - Infancy
  - Adolescence
  - Polycythemia Vera
- Malabsorption
  - Tropical Sprue
  - Gastrectomy
  - Chronic atrophic gastritis
- Dietary inadequacy (almost never sole cause)
- Combinations of above

Daily Iron Cycle

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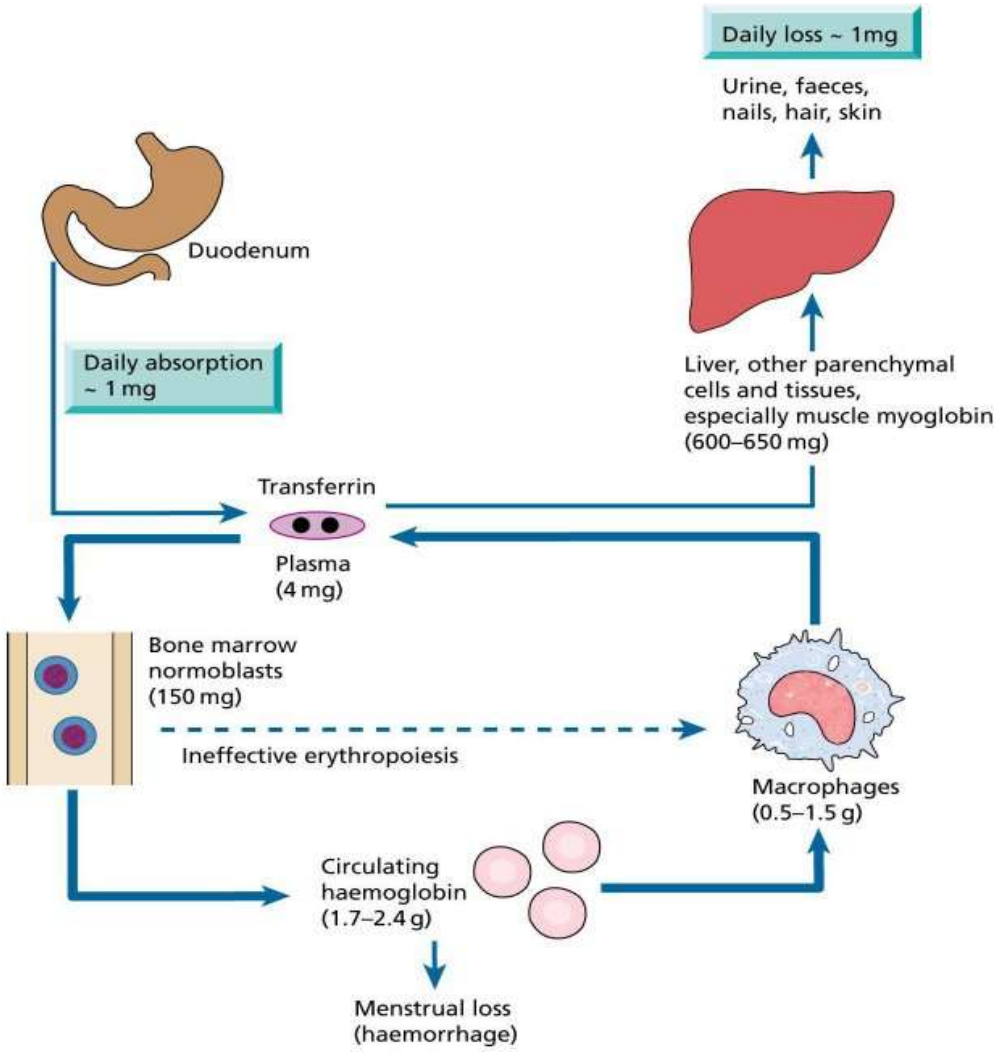

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1. Most of Iron in the Body is contained in circulating Hb

2. Iron is transferred from Macrophages to plasma transferrin then to BM Erythroblasts

3. Iron absorption is sufficient to Make up for iron loss

4. In iron deficiency tissue iron is less likely to become depleted than blood iron

5.

IRON

Body Compartments - 75 kg man

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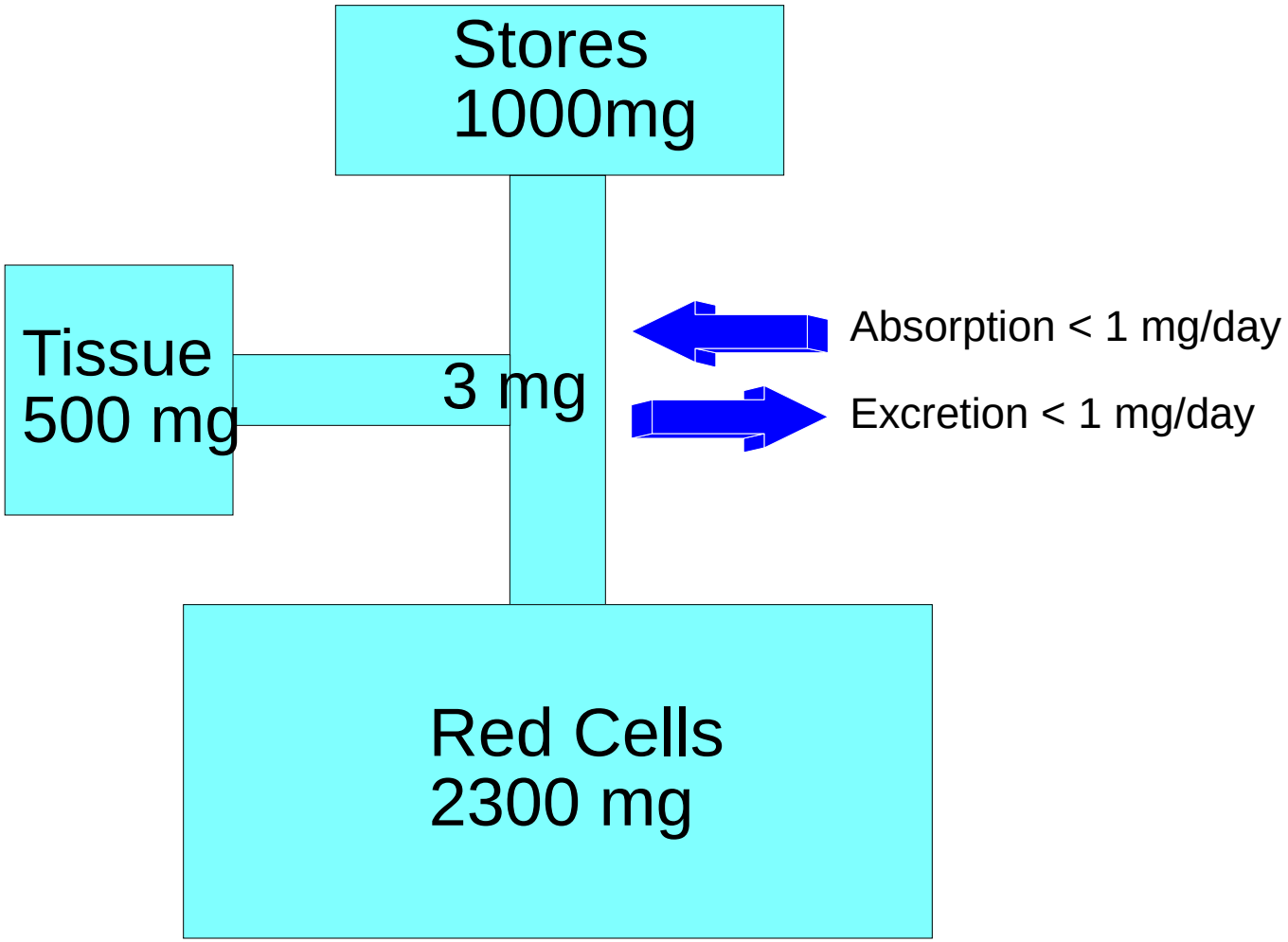

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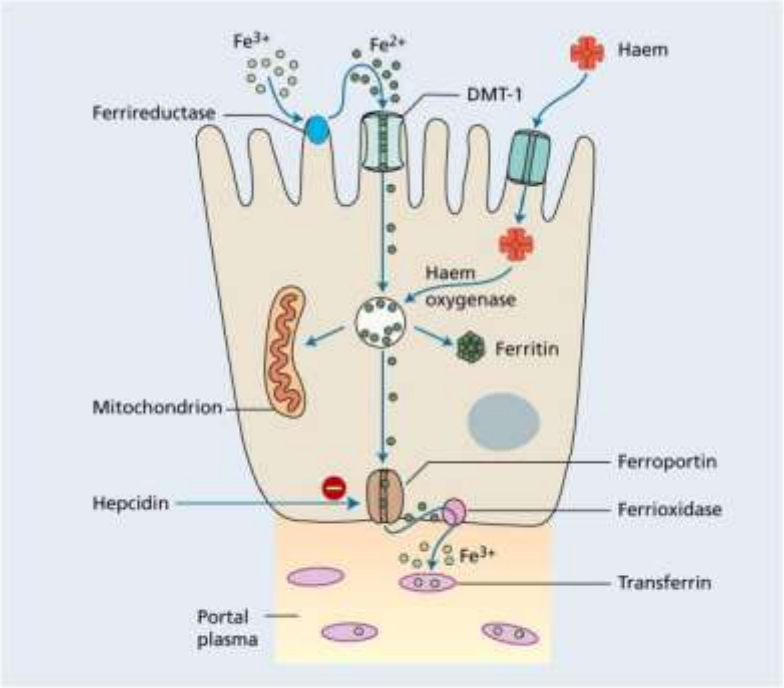
Iron cycle in the duodenum Enterocyte



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1. Fe+3 is reduced to Fe+2 by ferroreductase
2. Enter through the divalent cation binder DMT-1
3. Feroportin chanel protein control its transport to plasma
4. Oxidized by ferrooxidaze before binding to trasferrin

Transferrins are iron-binding blood plasma glycoproteins that control the level of free iron in biological fluids

Ferritin: is the major iron storage protein of the body, so measurement of ferritin levels is an indirect way to measure the amount of iron stored by the body. Ferritin has the shape of a hollow sphere that permits the entry of a variable amount of iron for storage (as ferric hydroxide phosphate complexes

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Table 3.1 The distribution of body iron.

Amount of iron in average adult	Male (g)	Female (g)	Percentage of total
Haemoglobin	2.4	1.7	65
Ferritin and haemosiderin	1.0 (0.3–1.5)	0.3 (0–1.0)	30
Myoglobin	0.15	0.12	3.5
Haem enzymes (e.g. cytochromes, catalase, peroxidases, flavoproteins)	0.02	0.015	0.5
Transferrin-bound iron	0.004	0.003	0.1

Daily Iron Requirments

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- Some Groups Demand on Iron is higher than others because of loss due to normal physiology or age.

Table 3.3 Estimated daily iron requirements. Units are mg/day.

	Urine, sweat, faeces	Menses	Pregnancy	Growth	Total
Adult male	0.5–1				0.5–1
Postmenopausal female	0.5–1				0.5–1
Menstruating female*	0.5–1	0.5–1			1–2
Pregnant female*	0.5–1		1–2		1.5–3
Children (average)	0.5			0.6	1.1
Female (age 12–15)*	0.5–1	0.5–1		0.6	1.6–2.6

* These groups are more likely to develop iron deficiency.

Iron stores are deprived completely before anemia development

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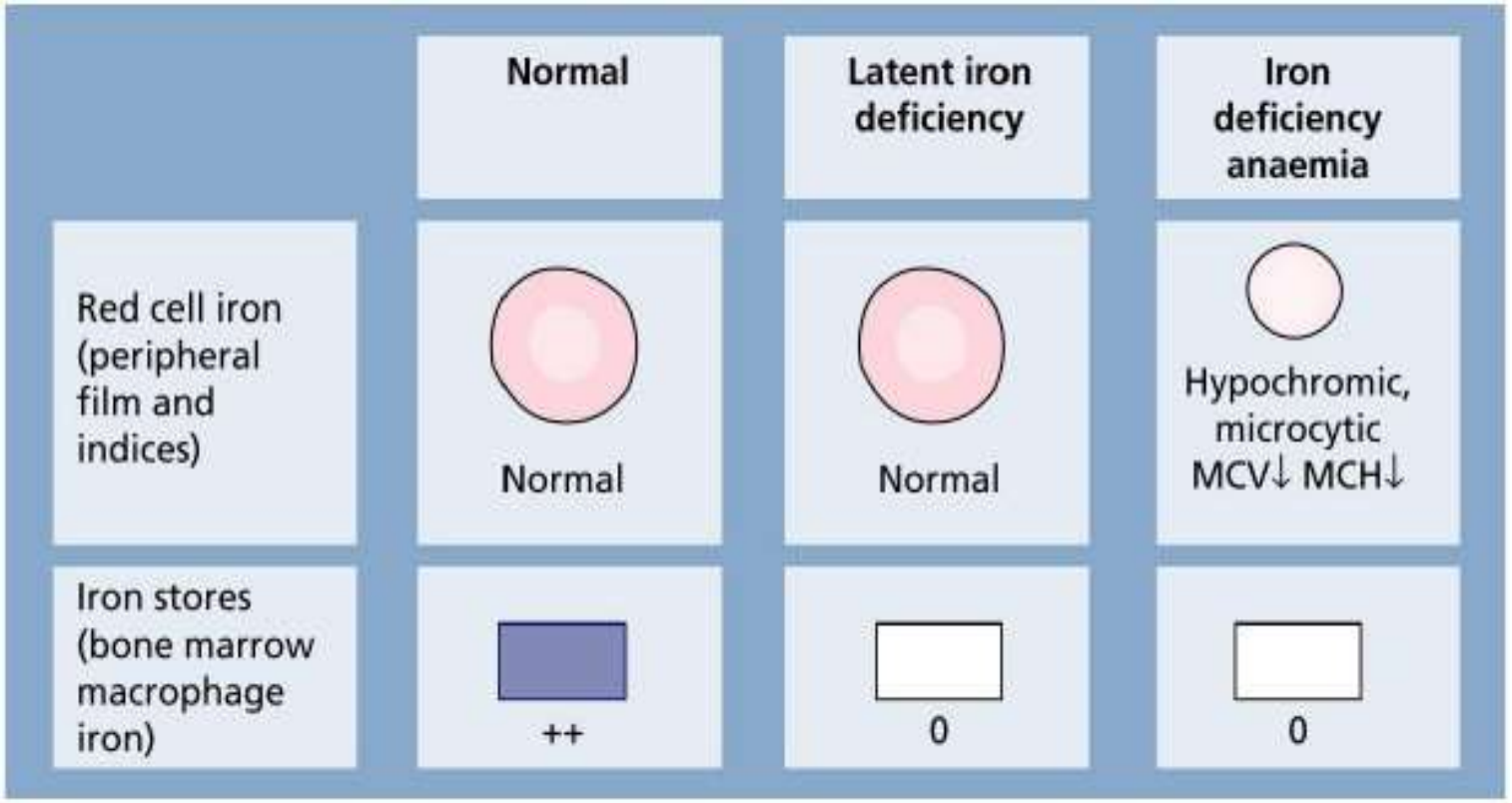

Major Symptoms of Iron Deficiency Anemia

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Koilonychia: spoon nail

(a)

Angular Cheilosis: ulceration of the corner of the mouth

(b)

Laboratory Findings

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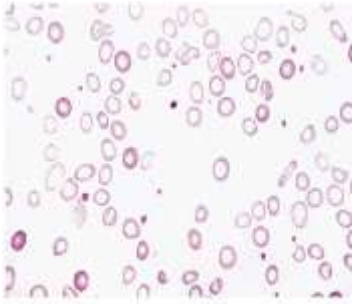
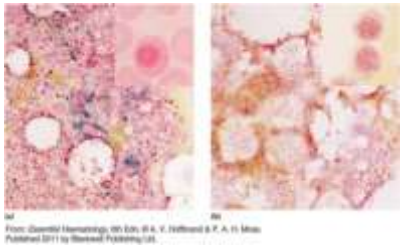


Blood film and indices

1. Fall in all indices mainly after sever anemia
   ↓MCV, ↓ MCH, ↓ MCHC
2. Hypochromic microcytic RBC with target cells occasionally



Bone Marrow Iron:
macrophage stores and erythroblasts are completely deprived

Serum Iron: below normal levels normal = 10-30 µmole/liter

Total Iron Binding Capacity (TIBC)= above normal
serum iron + unsaturated Iron binding capacity UIBC
normal range = 40-75 µmole/liter

Serum ferritin: reduced
normal male: 40-340 µg/l female: 14-150 µg/l
1 µg/l in serum reflects 8-10 mg reserved iron in tissues

Transferrin: normal level in serum is 2-4 g/l. 1 g/l = 20 µmole/liter binding capacity

TABLE 5
Hemoglobin and Hematocrit Values Diagnostic of Anemia

Gender/Age (yrs)	Hemoglobin<g/dL	Hematocrit<%
Females		
12-14.9	11.8	35.7
15-17.9	12.0	35.9
18+	12.0	35.9
Males		
12-14.9	12.5	37.3
15-17.9	13.3	39.7
18+	13.5	39.9

Laboratory Test	Value
Ferritin	<15 ug/L
Serum transferrin receptor concentration (TfR)	>8.5 mg/L
Transferrin saturation	<16%
Mean cell volume (MCV)	<82/85 fL*
Red cell distribution width (RDW)	>14%
Erythrocyte protoporphyrin (FEP)	>70 ug/dL

* <15 yrs/>15 yrs of age

Source: Centers for Disease Control and Prevention. Recommendations to prevent and control iron deficiency anemia in the United States. Morb Mortal Wkly Rep 1998; 47:1-29.

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FACTORS AFFECTING IRON ABSORBTION

Factors favouring absorption	Factors reducing absorption
Haem iron	Inorganic iron
Ferrous form (Fe^{2+})	Ferric form (Fe^{3+})
Acids (HCl, vitamin C)	Alkalis – antacids, pancreatic secretions
Solubilizing agents (e.g. sugars, amino acids)	Precipitating agents – phytates, phosphates, tea
Reduced serum hepcidin, e.g. iron deficiency	Increased serum hepcidin, e.g. iron excess
Ineffective erythropoiesis	Decreased erythropoiesis
Pregnancy	Inflammation
Hereditary haemochromatosis	
Increased expression of DMT-1 in duodenal enterocytes	Decreased expression of DMT-1 in duodenal enterocytes

TABLE 8
Dietary Factors That Enhance and Inhibit Iron Absorption

Enhance	Inhibit
Meat	Phosphate
Fish	Calcium
Poultry	Tea (tannic acid)
Seafood	Coffee
Gastric acid	Colas
Ascorbic acid	Soy protein
Malic acid	High doses of minerals
Citric acid	Bran/fiber

Source: Compiled from Provan D. Mechanisms and management of iron deficiency anaemia. Br J Haematol 1999; 105 Suppl 1:19-26; Wharton B. Iron deficiency in children: detection and prevention. Br J Haematol 1999; 106:270-280; Cook JD. The measurement of serum transferring receptor. Am J Med Sci 1999;318:269-276.

Anemia of Chronic Disorder

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In response to inflammatory cytokines, increasingly IL-6,the liver produces increased amounts of hepcidin. Hepcidin in turn causes increased internalisation of ferroportin molecules on cell membranes which prevents release from iron stores.

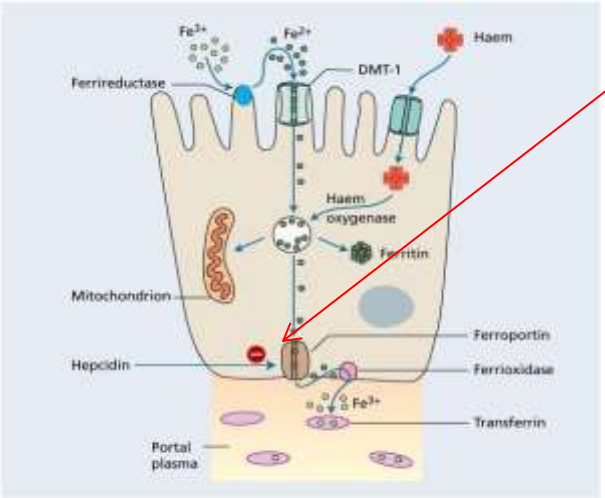

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Table 3.6 Causes of the anaemia of chronic disorders.

Chronic inflammatory diseases
Infections (e.g. pulmonary abscess, tuberculosis, osteomyelitis, pneumonia, bacterial endocarditis)
Non-infectious (e.g. rheumatoid arthritis, systemic lupus erythematosus and other connective tissue diseases, sarcoidosis, Crohn's disease, Gaucher's disease)
Malignant diseases
Carcinoma, lymphoma, sarcoma

Table 3.7 Laboratory diagnosis of a hypochromic anaemia.

	Iron deficiency	Chronic inflammation or malignancy	Thalassaemia trait (α or β)	Sideroblastic anaemia
MCV/ MCH	Reduced in relation to severity of anaemia	Normal or mild reduction	Reduced; very low for degree of anaemia	Usually low in congenital type but MCV usually raised in acquired type
Serum iron	Reduced	Reduced	Normal	Raised
TIBC	Raised	Reduced	Normal	Normal
Serum ferritin	Reduced	Normal or raised	Normal	Raised
Bone marrow iron stores	Absent	Present	Present	Present
Erythroblast iron	Absent	Absent	Present	Ring forms
Haemoglobin electrophoresis	Normal	Normal	Hb A_2 raised in β form	Normal

MCH, mean corpuscular haemoglobin; MCV, mean corpuscular volume; TIBC, total iron-binding capacity.

Anemia of Chronic Disorder

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Features:

1. Normocytic, Normochromic or mildly hypochromic (MCV<75 fl)
2. Mild and non-progressive anemia (Hb rarely less than 9.0g/dl)
3. Both serum and iron and TIBC are reduced
4. The serum ferritin is normal or raised
5. Bone marrow storage of iron is normal but erythroblast iron is reduced
6. The anemia is corrected by successful treatment of the underlying disease not by iron therapy

Sidroblastic Anemia

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1. Refractory anemia with hypochromic cells in peripheral blood and increase in marrow iron (due to defect in heam synthesis.
2. Diagnosed by the presence of many pathological ring sidroblast in the bone marrow.
3. Ring sidroblasts: abnormal RBC with Iron precipitated arranged in ring rather than distributed.