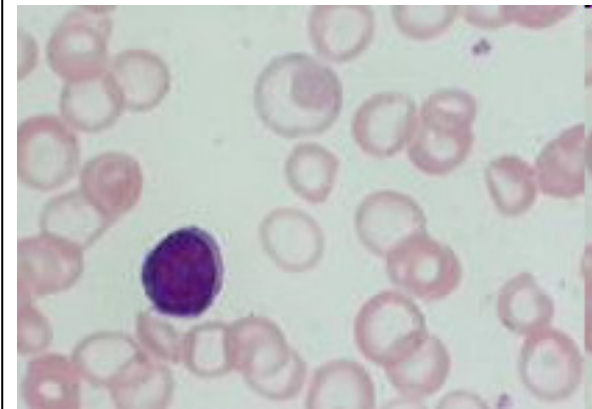


# **Iron deficiency anaemia and iron overload**

17-11-2009

# Iron deficiency anaemia

- Iron deficiency anemia is the most common of all anemias.
- Blood film shows microcytic hypochromic erythrocytes.
- Determining the cause of the Fe deficiency is of essential for proper treatment.
- Microcytic /hypochromic erythrocytes may also be seen in anemia of chronic disease, in thalassemia and in the sideroblastic anaemia.



Microcytic hypochromic RBCs.

# Causes of iron deficiency

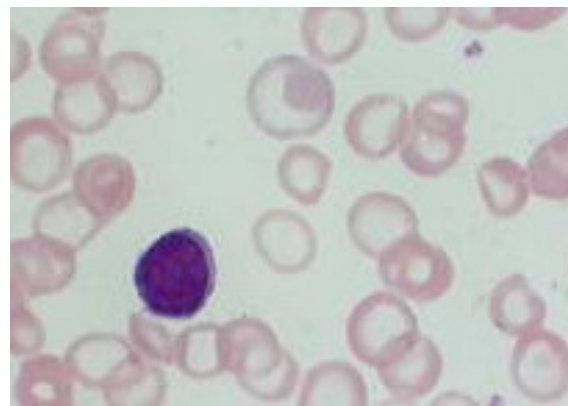
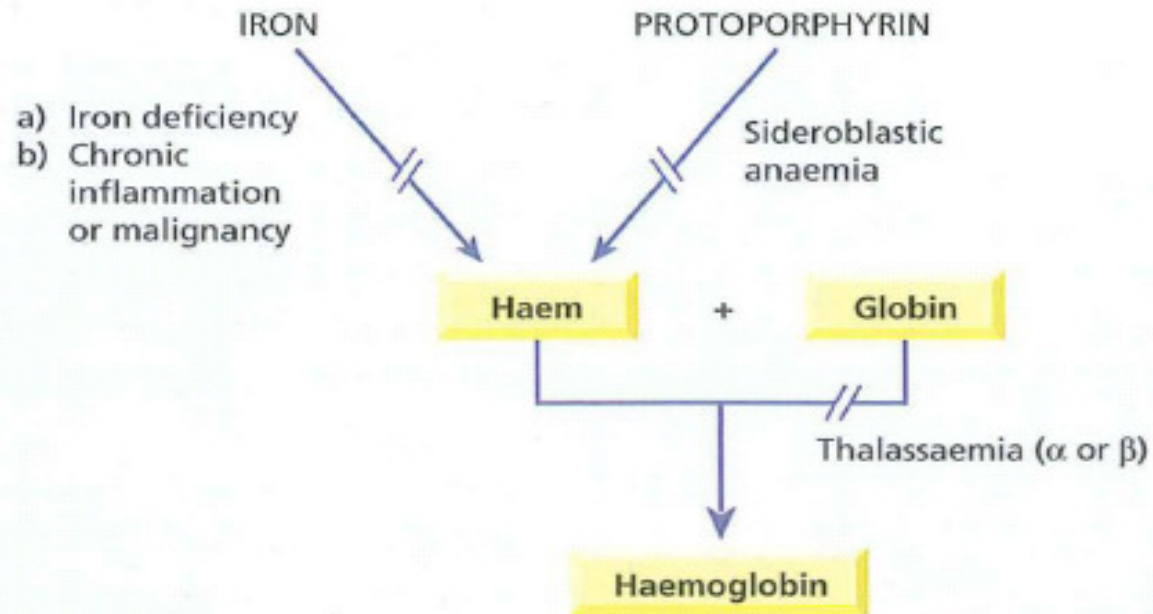
(1) Blood loss is the most common cause of iron deficiency.

- In women ages 15 to 45 years: menstruation is the most likely reason.
- In adult men and postmenopausal women: Iron deficiency anemia is most likely due to chronic gastrointestinal blood loss which is usually secondary to ulcers (peptic ulcer) or drugs (aspirin) or infections (parasitic infections), or inflammatory bowel disease and malignancy.

## Causes of iron deficiency

- (2) Lack of dietary iron may cause anemia in children. This is why iron supplements are given to infants. Iron deficiency is a major cause of anemia in pregnancy.
- (3) Malabsorption of iron is a rare cause of iron deficiency but is seen in patients who have had a partial gastrectomy or who have a malabsorption disorder.

# Causes of hypochromic microcytic anaemia

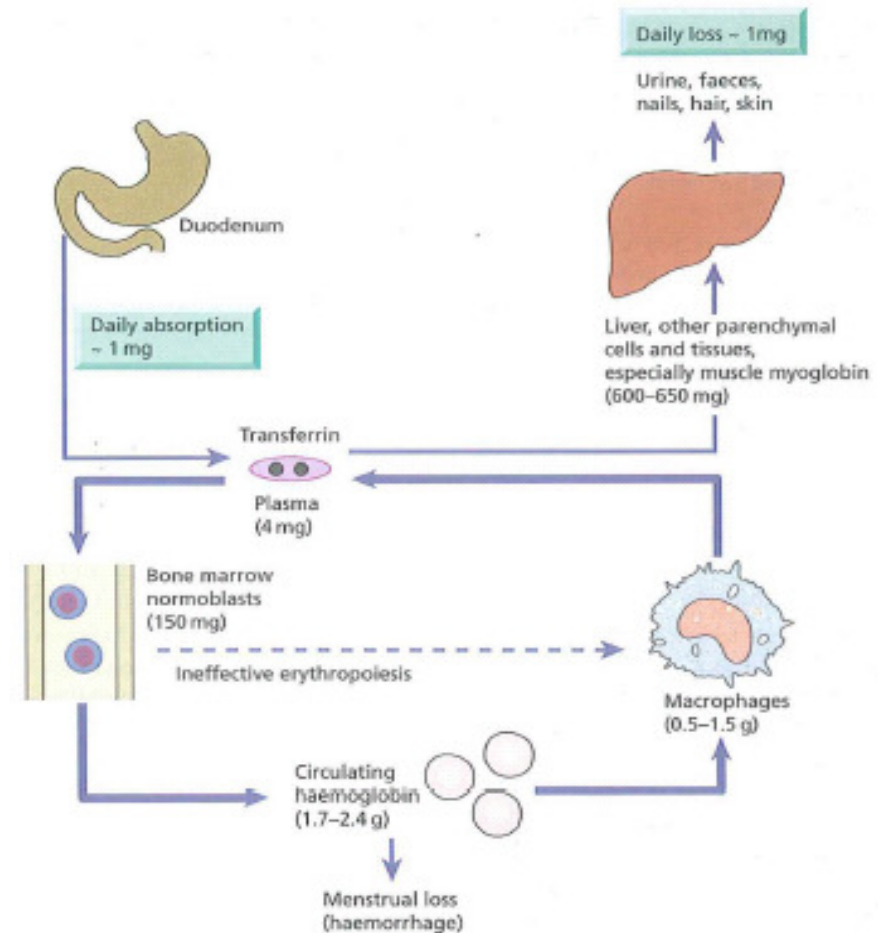


# Daily iron cycle

-Most of the iron in the body is contained in circulating haemoglobin and is reutilized for haemoglobin synthesis.

-after the red cells die, iron is transferred from macrophages to plasma transferrin and so to bone marrow erythroblasts.

-Iron absorption is normally just sufficient to make up for iron loss.



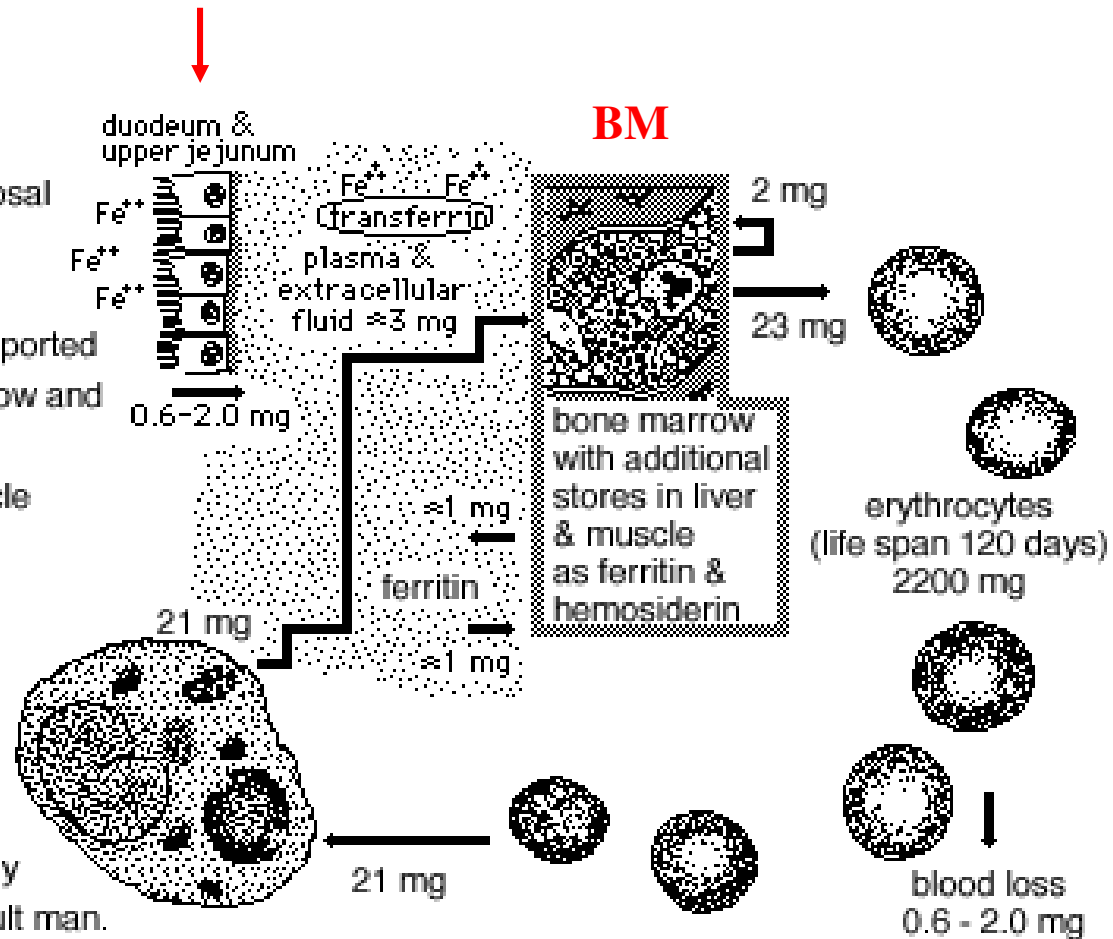
# iron cycle

## Absorption sites of iron

Iron enters the body via the GI mucosa, binding to a mucosal cell surface receptor.

Iron is oxidized to  $Fe^{+++}$ , bound to transferrin and transported through the blood to the marrow and other tissues.

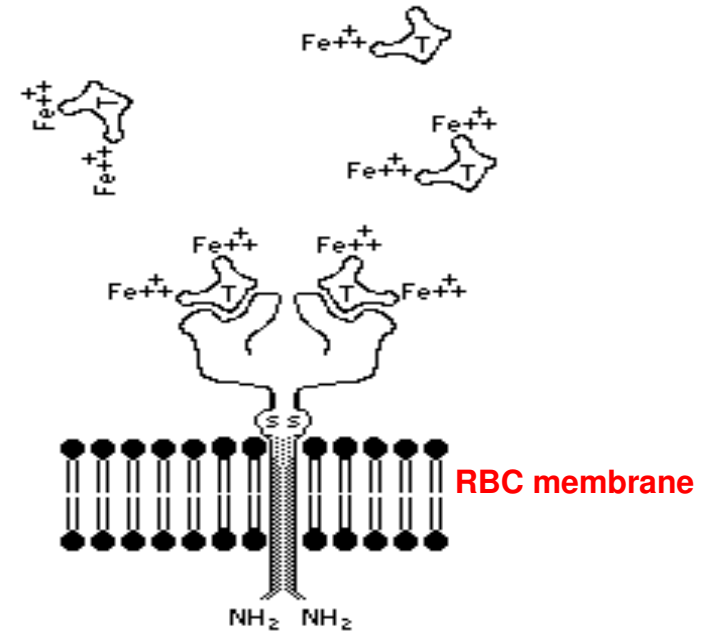
The normal internal iron cycle is a "closed" system.



The amounts shown are daily intake/loss in an average adult man.

# Iron transportation & metabolism

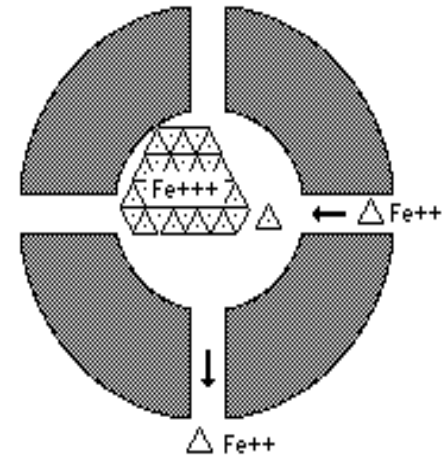
- **Transferrin**, the major iron transport protein, is synthesized by the liver and macrophages.
- Each molecule of transferrin can bind two atoms of iron.
- Usually about one-third (25 - 45%) of the total transferrin is bound to iron (referred to as % saturation).
- Transferrin carries iron via plasma to cells throughout the body, and mainly to the erythroblast cells in the BM.
- Transferrin binds to transferrin receptors (CD71) on the erythroblast surface membrane.
- Inside the cell, iron is released from transferrin as  $Fe^{++}$  (ferrous) and transported to mitochondria where it is complexed with protoporphyrin IX to form heme.





# Ferritin

- Free iron is toxic to cells.
- **Ferritin** is the primary intracellular iron-storage protein.
- It stores iron and releases it in a controlled fashion.
- Small amounts of ferritin, derived from iron stores, circulate in the plasma and take up excess iron (storage) and release it when needed.
- It is a buffer against iron deficiency and iron overload.
- The amount of serum ferritin closely reflects iron stores, thus providing a readily measured assessment of body iron stores.
- Ferritin level increases in liver disease, malignancy, and chronic inflammation.
- Serum ferritin (30-300 ng/mL) is the most sensitive lab test for iron deficiency anemia.



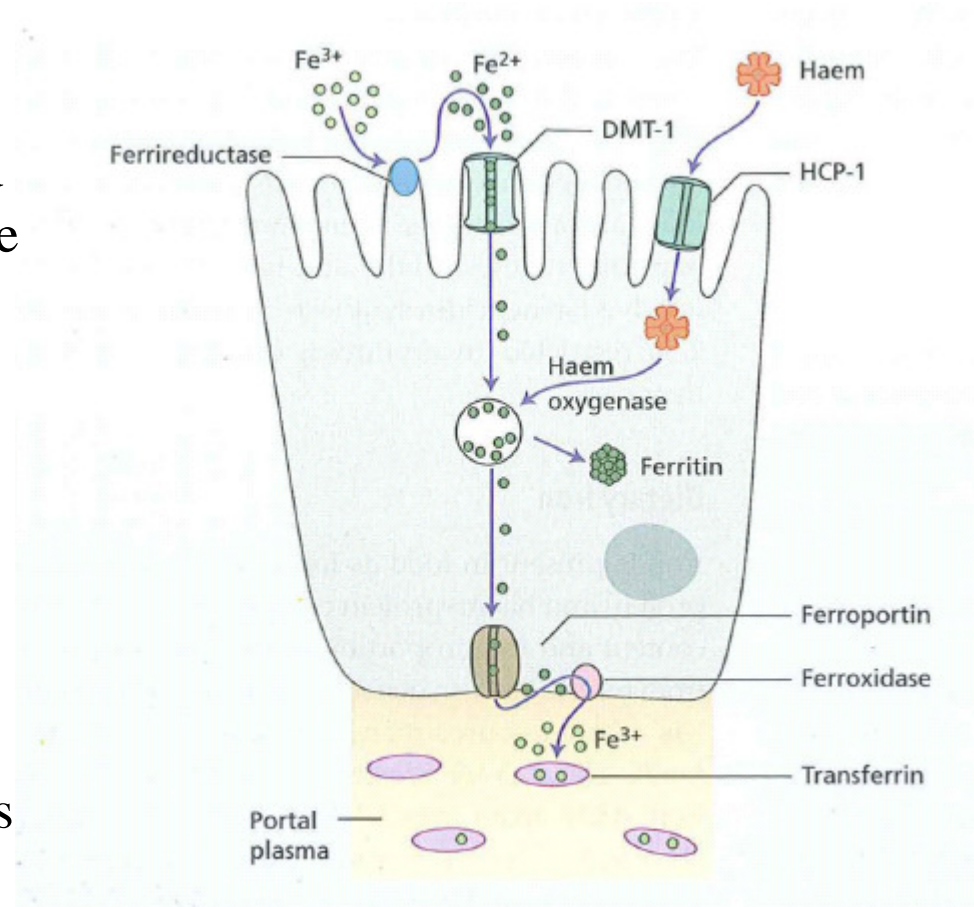
# Iron absorption

Table 3.2 Iron absorption.




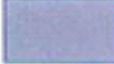


Factors favouring absorption	Factors reducing absorption
Haem iron	Inorganic iron
Ferrous form ( $\text{Fe}^{2+}$ )	Ferric form ( $\text{Fe}^{3+}$ )
Acids (HCl, vitamin C)	Alkalis—antacids, pancreatic secretions
Solubilizing agents (e.g. sugars, amino acids)	Precipitating agents—phytates, phosphates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

# The regulation of iron absorption

- 
- Dietary ferric ( $\text{Fe}^{3+}$ ) iron is reduced to  $\text{Fe}^{2+}$  and its entry to the enterocyte is through the divalent cation binder DMT-1.
- Its export into portal plasma is controlled by ferroportin.
- It is oxidized before binding to transferrin in plasma.
- Haem is absorbed after binding to its receptor protein Hep-I.



# The development iron deficiency anaemia

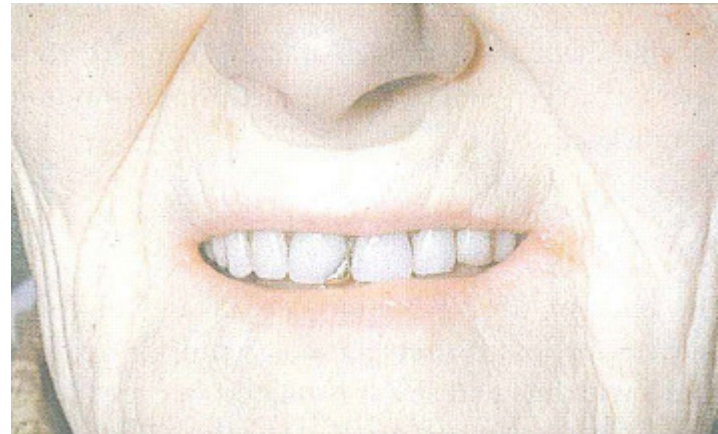
	Normal	Latent iron deficiency	Iron deficiency anaemia
Red cell iron (peripheral film and indices)	 Normal	 Normal	 Hypochromic, microcytic MCV↓ MCH↓
Iron stores (bone marrow macrophage iron)	 ++	 0	 0

Macrophage stores are lost completely before Iron stores anaemia develops

# Iron deficiency anaemia



Koilonychia: typical 'spoon' nails



Angular cheilosis: fissuring and ulceration of the corner of the mouth.



# Causes of iron deficiency

Table 3.4 Causes of iron deficiency.

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*Chronic blood loss*

Uterine

Gastrointestinal, e.g. peptic ulcer, oesophageal varices, aspirin (or other non-steroidal anti-inflammatory drugs) ingestion, partial gastrectomy, carcinoma of the stomach, caecum, colon or rectum, hookworm, angiodysplasia, colitis, piles, diverticulosis

Rarely, haematuria, haemoglobinuria, pulmonary haemosiderosis, self-inflicted blood loss

*Increased demands* (see also Table 3.3)

Prematurity

Growth

Pregnancy

Erythropoietin therapy

*Malabsorption*

Gluten-induced enteropathy, gastrectomy

*Poor diet*

A contributory factor in many developing countries but rarely the sole cause except in infants and children

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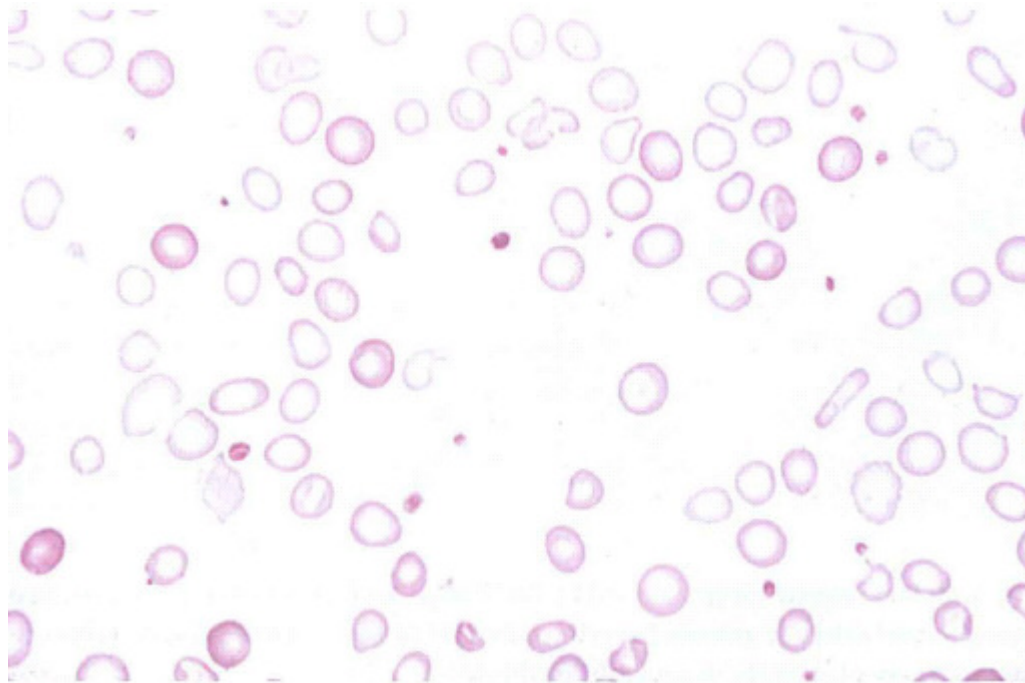
- **Total iron-binding capacity (TIBC)** is a medical laboratory test which measures the blood's capacity to bind iron with transferrin.

# Laboratory findings of iron deficiency anaemia

- The blood film shows hypochromic microcytic cells with occasional target cells and pencil-shaped poikilocytes.
- Red cell indices are low (MCV, MCH).
- The reticulocyte count is low.
- The platelet count is moderately raised.
- **BM:** complete absence of iron from stores (macrophages) and from developing erythroblasts.
- Serum ferritin is very low.
- Low serum iron.
- High levels of total iron-binding capacity (TIBC).
- The level of serum transferrin receptor (sTfR) is Increased.

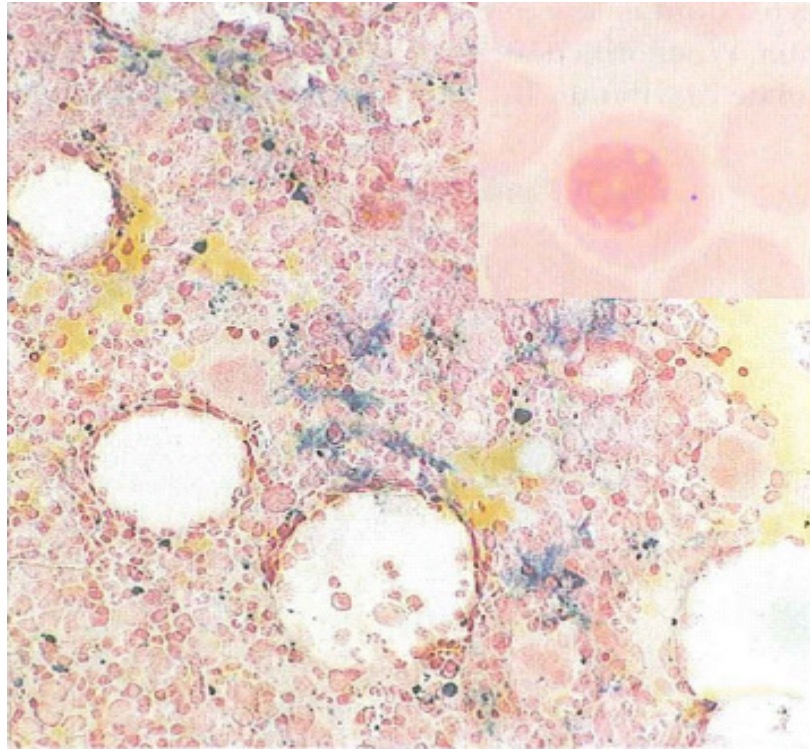


# blood film in severe iron deficiency anaemia



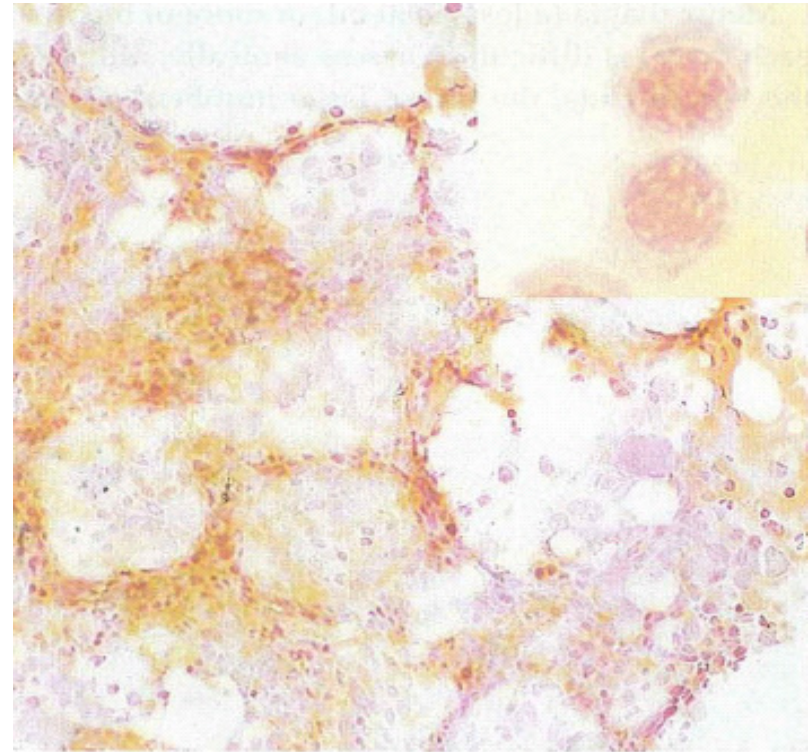
The cells are microcytic and hypochromic with occasional target cells.

## Bone marrow iron assessed by Perls' (Prussian blue) stain



Normal iron stores indicated by blue staining in the macrophages.

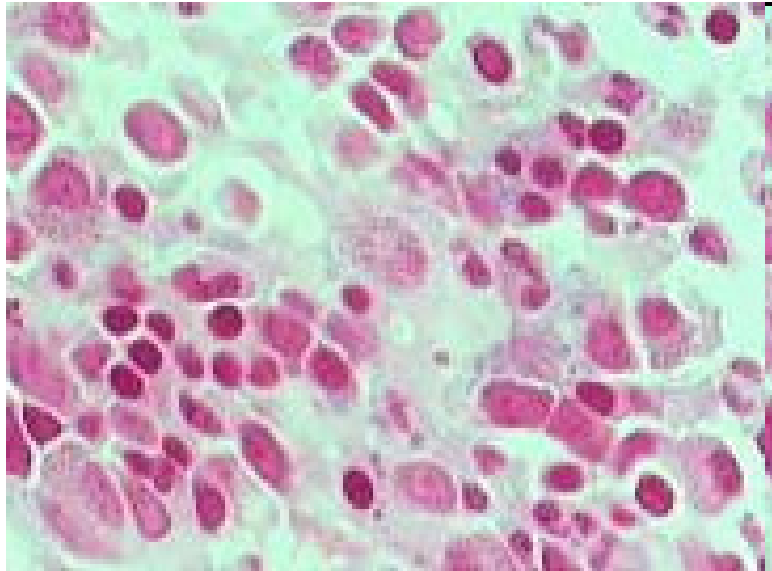
**Inset:** normal siderotic granule in erythroblast.



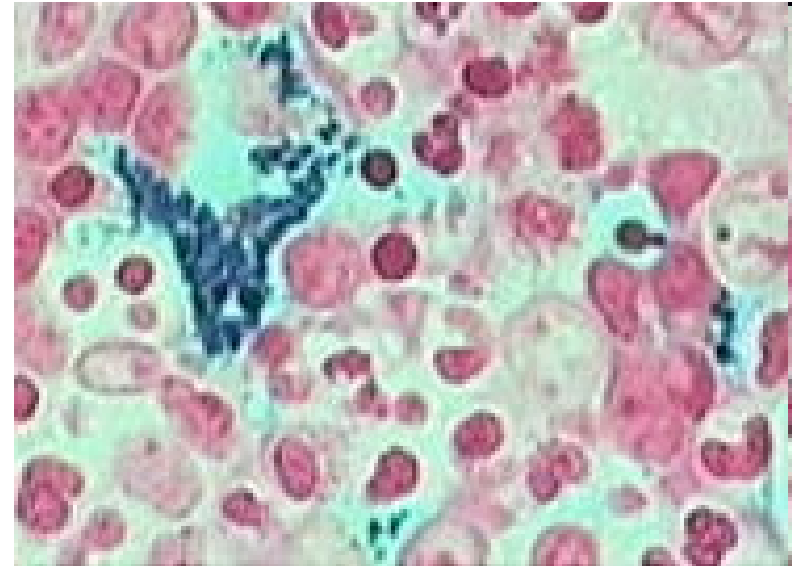
Absence of blue staining (absence of haemosiderin) in iron deficiency.

**Inset:** absence of siderotic granules in erythroblasts.

# The definitive test for iron deficiency is a Prussian blue (Perl's) stained bone marrow



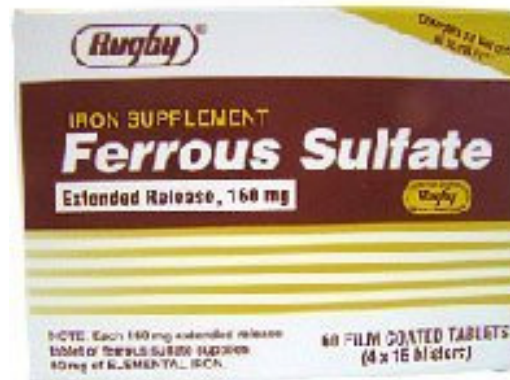
Absence of iron in the bone marrow macrophages of an individual with iron deficiency.



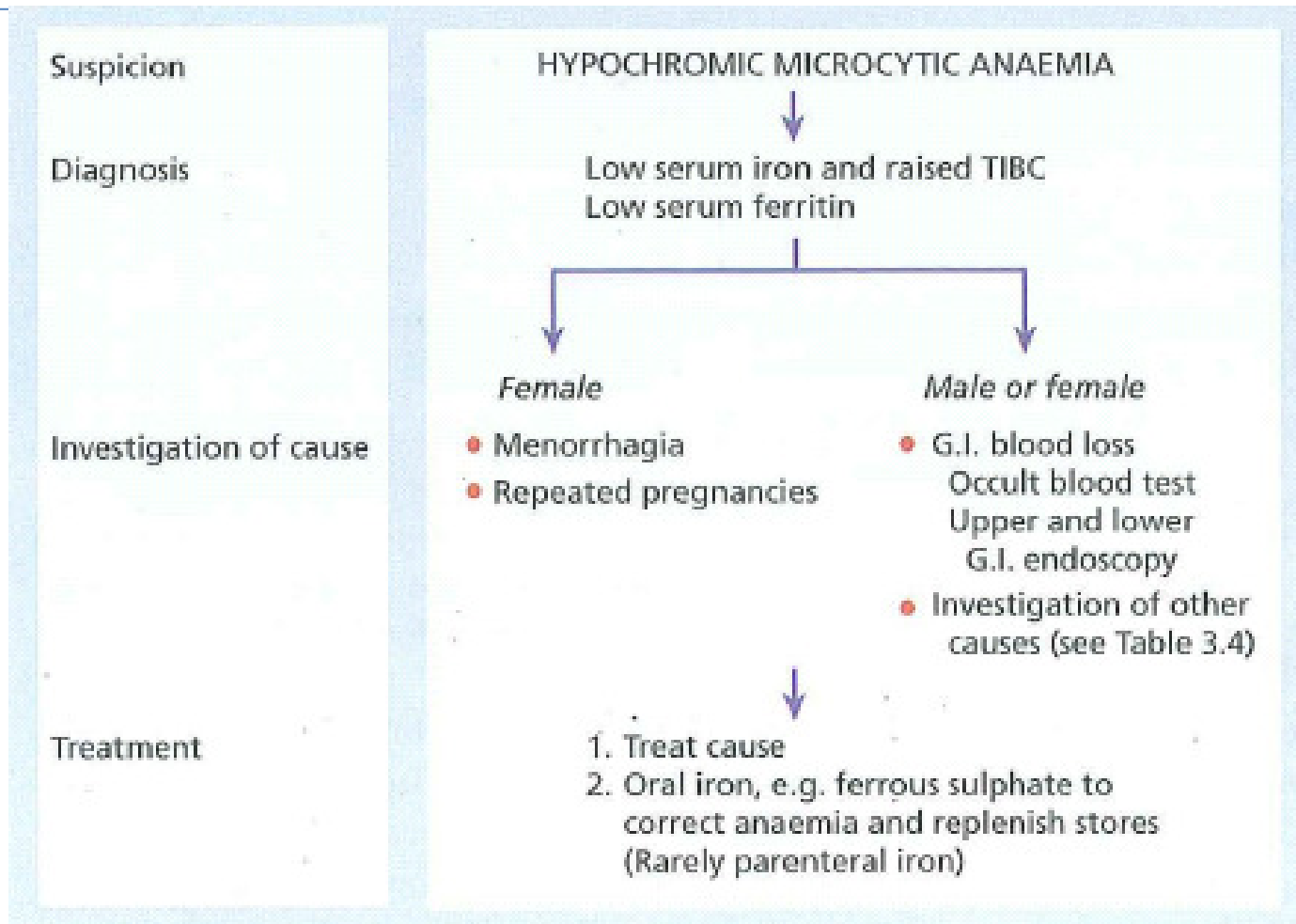
Normal bone marrow stained with Prussian blue and demonstrating coarse granular storage iron in macrophages

# Treatment of iron deficiency anaemia

- The oral administration of ferrous sulfate is the usual therapy for Fe deficiency.



# Investigation and management of iron deficiency anaemia



# Anaemia of chronic diseases

Table 3.6 Causes of the anaemia of chronic disorders.

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*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)

*Malignant diseases*

Carcinoma, lymphoma, sarcoma

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# Laboratory diagnosis of a hypochromic anaemia

Table 3.7 Laboratory diagnosis of a hypochromic anaemia.

	Iron deficiency	Chronic inflammation or malignancy
MCV MCH	Reduced in relation to severity of anaemia	Normal or mild reduction
Serum iron	Reduced	Reduced
TIBC	Raised	Reduced
Serum transferrin receptor	Raised	Normal/low
Serum ferritin	Reduced	Normal or raised
Bone marrow iron stores	Absent	Present
Erythroblast iron	Absent	Absent
Haemoglobin electrophoresis	Normal	Normal



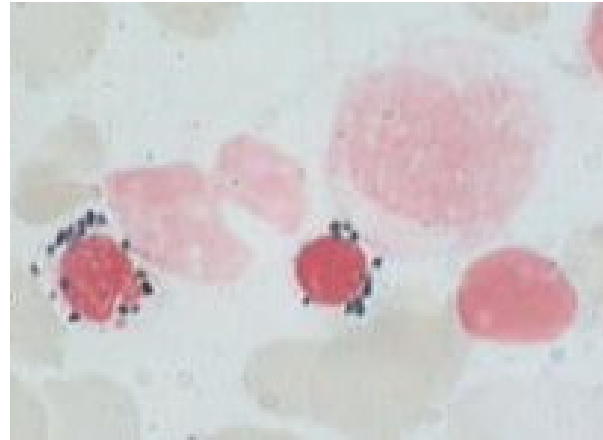
# Sideroblastic anaemia



- Sideroblastic anemias are usually associated with microcytosis and hypochromia and thus must be distinguished from the anemias of iron deficiency and thalassemia.
- Although adequate iron is present, a mitochondrial defect (decreased activity of D-ALA or ferrochelatase) prevents the incorporation of iron into hemoglobin.
- Instead iron accumulates in mitochondria ringing the erythroblasts nucleus forming "ringed sideroblasts".
- Sideroblasts are erythroblasts with non-heme iron-containing organelles.
- Most sideroblastic anemias are acquired and are associated with drugs (alcohol).
- Hereditary sideroblastic anemias are usually microcytic/hypochromic and thus must be distinguished from iron deficiency and thalassemia.
- Blood transfusions may be necessary because of the ineffective erythropoiesis of sideroblastic anemia.



# Sideroblastic anaemia



Ring sideroblasts with a perinuclear ring of iron granules in sideroblastic anaemia

# Iron overload

- There is no physiological mechanism for eliminating excess iron from the body.
- Iron absorption is normally carefully regulated to avoid accumulation.
- Iron overload can occur in disorders associated with excessive absorption or chronic blood transfusion.
- Excessive iron deposition in tissues can cause serious damage to organs, particularly the heart, liver and endocrine organs.

# The causes of iron overload

**Table 3.9** The causes of iron overload.

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Increased iron absorption	Hereditary (primary) haemochromatosis Ineffective erythropoiesis, e.g. thalassaemia intermedia, sideroblastic anaemia Chronic liver disease
Increased iron intake	African siderosis (dietary and genetic)
Repeated red cell transfusions	Transfusion siderosis

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