Lecture_3

Iron deficiency anaemia

Fourth year students

Dentistry

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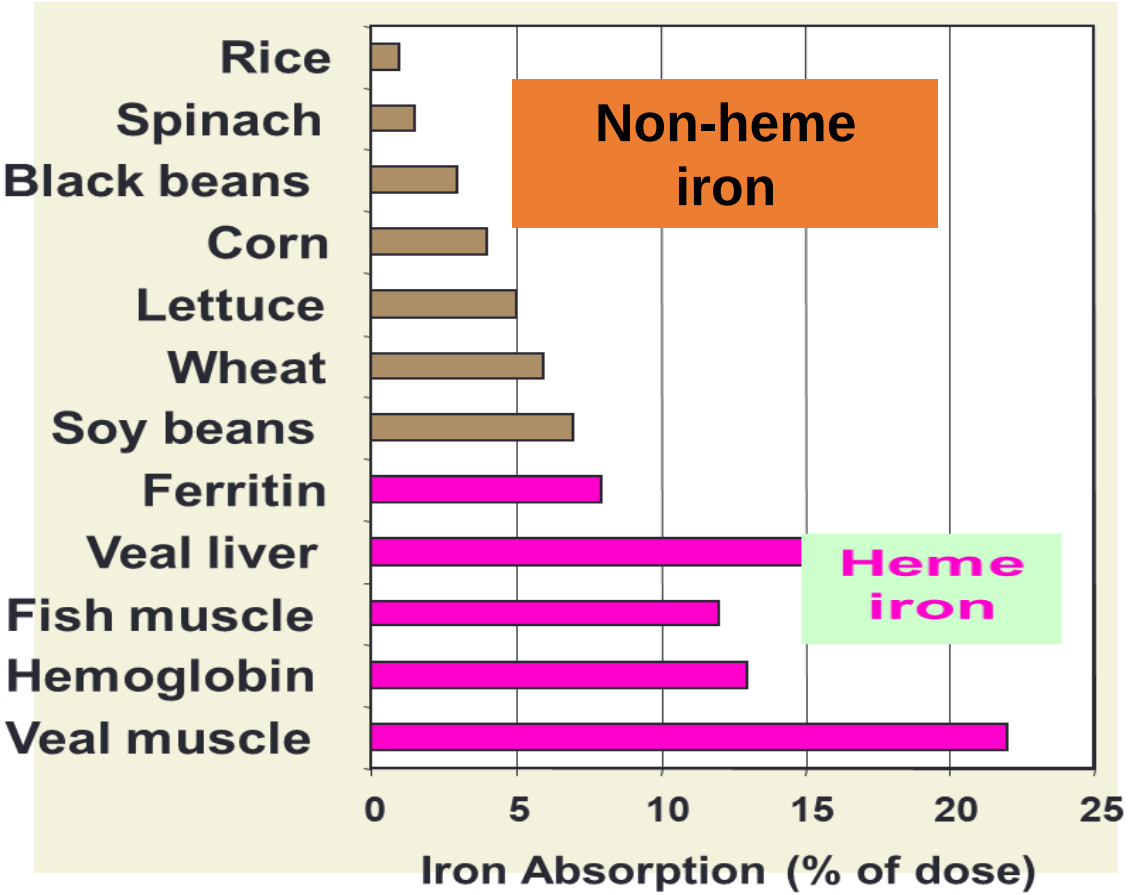
Presenting problems in blood disease

Anaemia

- a condition in which there is a deficiency of RBCs or of Hb in the blood, resulting in pallor and Fatigue
- The main consequence of anaemia is the in decrease oxygen supply to the tissues.
- A rapid onset of anaemia (e.g. due to blood loss) causes more profound symptoms than a gradually developing anaemia.

Iron: Dietary Sources

- average American diet: 10-50 mg iron
- **heme iron** – readily absorbed
  - animal source: meat, fish and poultry
  - not found in milk or dairy products
- **non-heme iron** – not readily absorbed
  - source: mostly plant products which contains phytates, tannins, oxalates that chelates / precipitates iron
  - iron supplements



- Normally iron is absorbed from the **proximal small intestine**; it is transported in the cell bound to the plasma bound to **transferrin**, later **transferrin receptor** maintain the uptake of iron by the RBC precursors
- Iron outside Hb-producing cells is stored in **ferritin** in liver, bone marrow, spleen, and muscle
- The total-body iron conc.
    - in men **50** mg/kg
    - In women is and **40** mg/kg

- **60% -75%** of the iron is found in Hb
- **2 mg/kg** is found in heme and nonheme enzymes
- **5 mg/kg** is found in myoglobin
- The capacity for excreting iron is limited, and iron overload occurs in patients with excessive absorption from the GIT and in those with chronic transfusions
- Iron deposition in endocrine organs, resulting in liver dysfunction, diabetes, and other endocrine abnormalities

factors known to enhance nonheme iron absorption

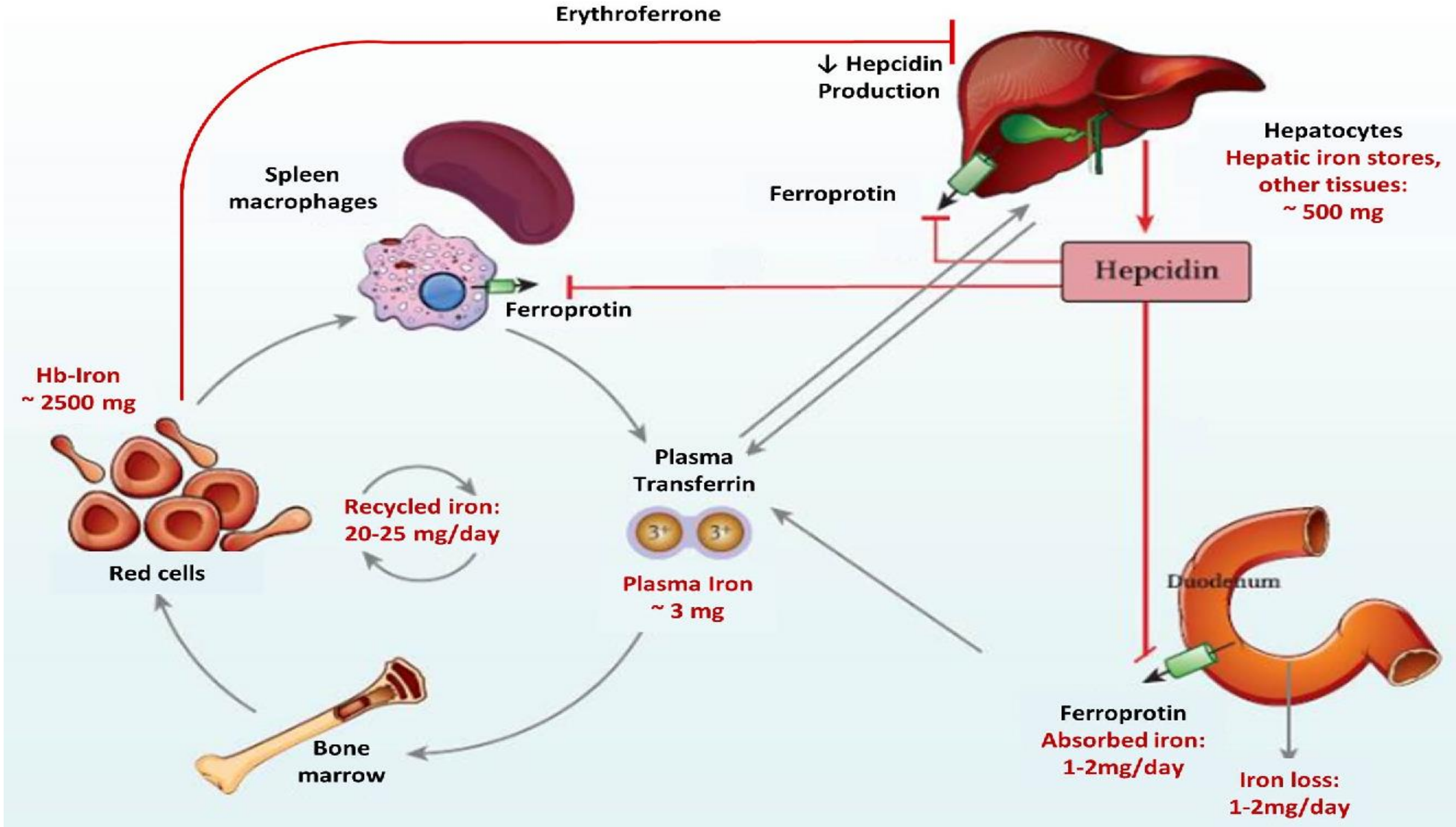
- MFP Factor (animal protein Meat – Fish – Poultry)
- Vitamin C
- Acids
- Sugars (Fructose)

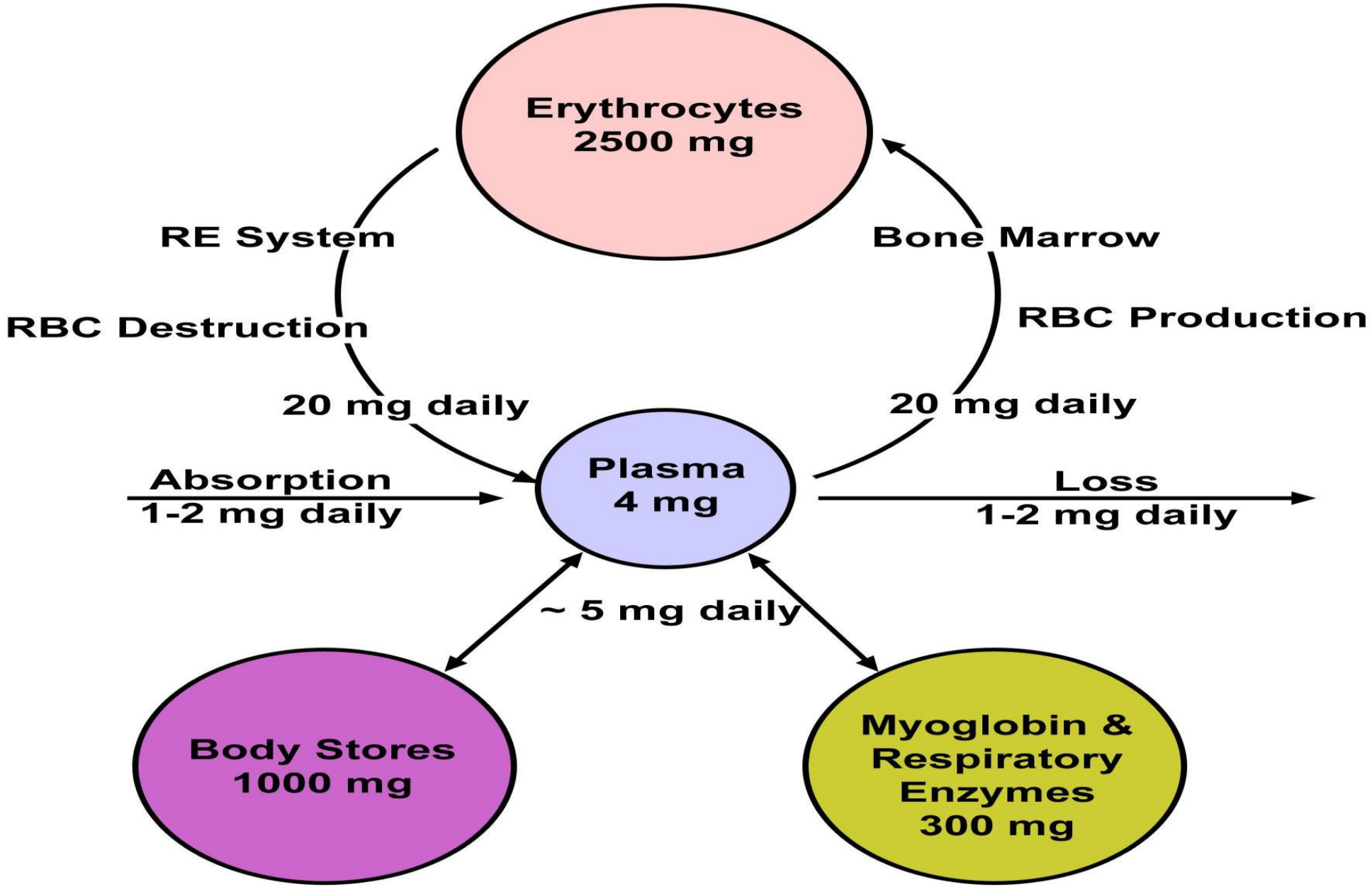
factors inhibit nonheme iron absorption

Phytates (legumes, grains, and rice)

- Vegetable proteins
- Tannic acid and other polyphenols in tea and coffee
- Calcium

  Milk Anaemia: The condition of developing iron-deficiency anaemia because milk (which is not an adequate source of iron) displaces iron-rich foods
- oxalic acid, zinc
- eggs


Erythroferrone
↓ Hepcidin Production
Hepatocytes
Hepatic iron stores, other tissues: ~ 500 mg
Spleen macrophages
Ferroprotin
Hepcidin
Ferroprotin
Hb-Iron ~ 2500 mg
Plasma Transferrin
Recycled iron: 20-25 mg/day
Red cells
Plasma Iron ~ 3 mg
Duodenum
Bone marrow
Ferroprotin
Absorbed iron: 1-2mg/day
Iron loss: 1-2mg/day


Erythrocytes
2500 mg
RE System
RBC Destruction
20 mg daily
Bone Marrow
RBC Production
20 mg daily
Absorption
1-2 mg daily
Plasma
4 mg
Loss
1-2 mg daily
~ 5 mg daily
Body Stores
1000 mg
Myoglobin &
Respiratory
Enzymes
300 mg

Iron Deficiency Anemia (IDA)

- IDA is the leading cause of anaemia worldwide
- Iron deficiency should be considered in all patients with anaemia

Causes of IDA

1) Blood loss

- The most common cause for IDA is gastrointestinal blood loss
  - occult gastric or colorectal malignancy, gastritis, peptic ulceration, inflammatory bowel disease, diverticulitis, polyps and angiodysplastic lesions.
  - Hookworm and schistosomiasis infestation of GI
  - Chronic use of aspirin or NSAIDs, which cause intestinal erosions and impair platelet function

- In women of child-bearing age, menstrual blood loss, pregnancy and breastfeeding contribute to iron deficiency by depleting iron stores

- Menstrual loss (~ 15 mg/month) and (900 mg per pregnancy)

- Very rarely, chronic haemoptysis or haematuria may cause iron deficiency

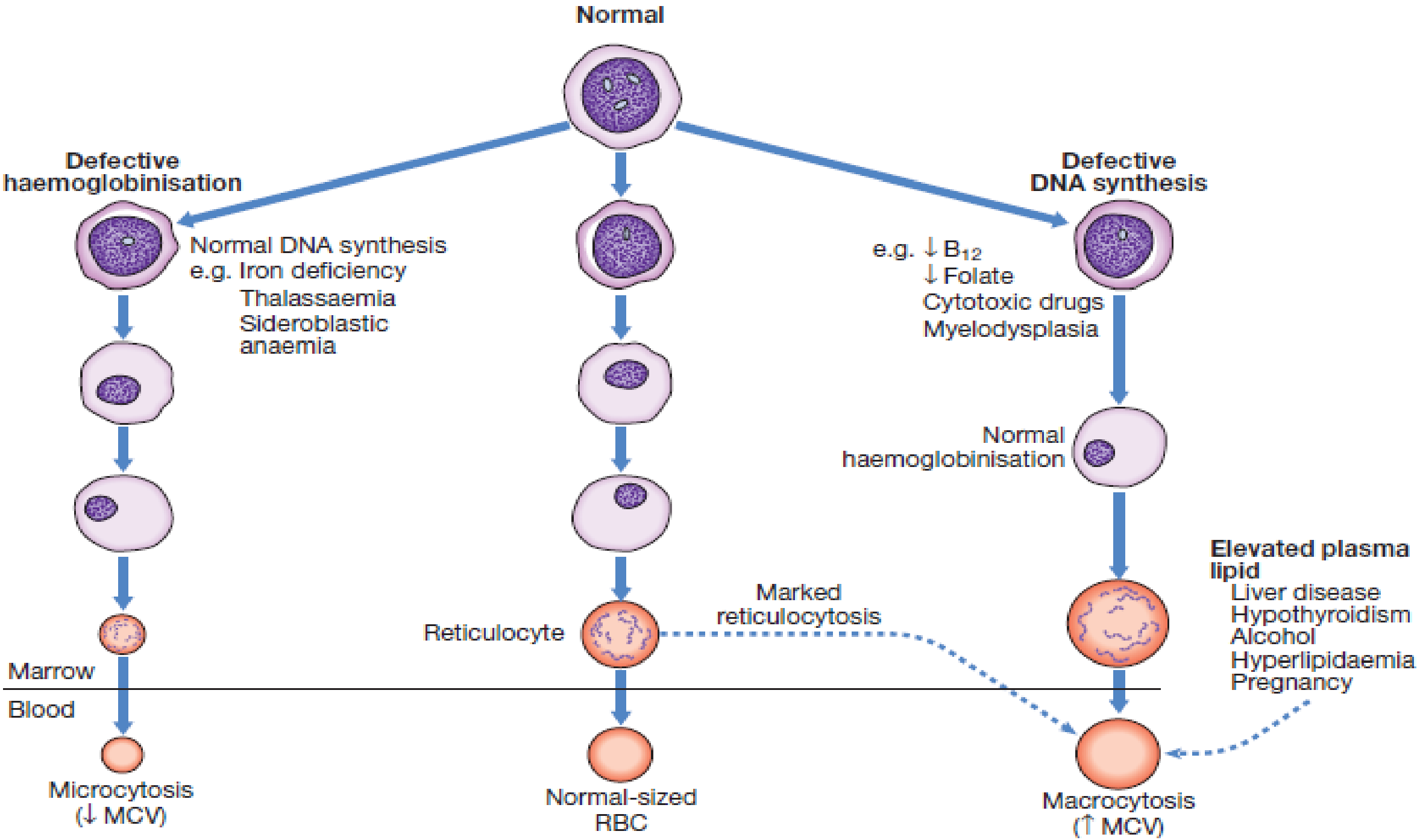
2) Malabsorption

- Normally gastric acid is required to release iron from food and helps to keep iron in the soluble ferrous state
- **Achlorhydria** (is a state of absent or low hydrochloric acid in the stomach) Occur in the elderly, previous gastric surgery or due to chronic drug use such as proton pump inhibitors that may contribute to the lack of iron availability from the diet
- Iron is absorbed actively in the upper small intestine and hence can be affected by coeliac disease

3. **Helicobacter pylori** infection of gastric or duodenal mucosa causing gastritis and sometimes duodenal ulcer can cause IDA even in the absence of intestinal bleeding

4. **Physiological demands**

- Rapid growth, such as infancy and puberty, where the requirement exceed the usual iron absorption
- babies who drink mostly milk at the expense of an intake of iron containing foods
- In pregnancy, iron is diverted to the foetus, the placenta and the increased maternal red cell mass, and is lost with bleeding at delivery


Normal
Defective haemoglobinisation
Normal DNA synthesis
e.g. Iron deficiency
Thalassaemia
Sideroblastic anaemia
Defective DNA synthesis
e.g. ↓ B_{12}
↓ Folate
Cytotoxic drugs
Myelodysplasia
Normal haemoglobinisation
Marrow
Blood
Reticulocyte
Marked reticulocytosis
Elevated plasma lipid
Liver disease
Hypothyroidism
Alcohol
Hyperlipidaemia
Pregnancy
Microcytosis (↓ MCV)
Normal-sized RBC
Macrocytosis (↑ MCV)

Clinical features

- Easy Fatigue and tiredness
- Leg cramps on climbing stairs
- Craving ice (in some cases, cold celery or other cold vegetables) to suck or chew
- Dysphagia with solid foods (esophageal web-Plummer Vinson Syndrome)
- Worsened symptoms of comorbid cardiac or pulmonary disease

On exam:

- Pallor
- Spoon-shaped nails (koilonychia)
- A glossy tongue, with atrophy of the lingual papillae
- Fissures at the corners of the mouth (angular stomatitis)

Investigations

1. General test : CBC
2. Confirmation of iron deficiency
    1. **Serum ferritin**

- is a measure of iron stores in tissues
    - It is the best single test to confirm iron deficiency
    - It is a very specific test

    - *Ferritin levels can be raised in liver disease and in the acute phase response*

2) **Plasma iron**

3) **total iron binding capacity (TIBC)**

- Both are measures of iron availability; and can be affected by many factors besides iron stores.

- Plasma iron has a marked diurnal and day-to-day variation and becomes very low during an acute phase response but is raised in liver disease and haemolysis

- Transferrin level, the binding protein for iron, are decreased by malnutrition, liver disease and nephrotic syndrome

4) Transferrin saturation (= iron/TIBC × 100)

- If < 16% is consistent with iron deficiency
- It is less specific than a ferritin measurement
- All proliferating cells express membrane transferrin receptors to acquire iron

5) **Plasma transferrin receptors** are blood proteins, may be elevated in persons with IDA

When there is low Iron store:

- Up-regulation transferrin receptors
- Increase in the levels of soluble plasma transferrin receptors

Investigation of the cause This depends on:

- The patients' characteristics (age and sex)
- Hx and clinical findings

- In men and in post-menopausal women with a normal diet, the upper and lower GIT should be investigated by endoscopy or radiological studies
- Serum anti-transglutaminase antibodies and a duodenal biopsy are required to diagnose coeliac disease
- In the tropics, stool and urine should be examined for parasites
- In difficult cases, it may still be necessary to examine a bone marrow aspirate for iron stores

Management

- Blood transfusion is not manditary and oral iron replacement is appropriate, except in certain situation:
    - patient has angina
    - heart failure
    - evidence of cerebral hypoxia

- Ferrous sulphate 200 mg 3 times daily (195 mg of elemental iron per day) is adequate and should be continued for **3–6** months to replete iron stores

- side-effects include: GI upset as *dyspepsia and altered bowel habit* which can be improved by reducing the dose to 200 mg twice daily or a switch to **ferrous gluconate** 300 mg twice daily (70 mg of elemental iron per day) or another alternative oral preparation should be tried

- A failure to respond adequately may be due to
  - non-adherence
  - continued blood loss
  - malabsorption or an
  - incorrect diagnosis
- Patients with malabsorption, chronic gut disease or inability to tolerate any oral preparation may need
- parenteral iron therapy.

Response to oral Iron Therapy

- Peak reticulocyte count 7 - 10 day
- Increased Hb and Hct 14 - 21 day
- Normal Hb and Hct 2 months
- Normal iron stores 4 - 5 months

- Previously, iron dextran or iron sucrose was used, but new preparations of iron isomaltose and iron carboxymaltose have fewer allergic effects and are preferred.
- Doses required can be calculated based on the patient’s starting haemoglobin and body weight
- Observation for anaphylaxis following an initial test dose is recommended.

Anaemia of chronic inflammation (AI)

previously known as anaemia of chronic disease (ACD)

is a common type of anaemia, particularly in hospital populations.

- occurs in patients with chronic inflammatory, infectious, malignant, or autoimmune disorders.
- Anaemia is not related to bleeding, haemolysis or marrow infiltration
- Usualy is mild, with
- Hb in the range of 85–115 g/L, with a normal MCV (normocytic, normochromic
- The serum iron is low but iron stores are normal or increased

Investigations to differentiate AI from IAD

	Ferritin	Iron	TIBC	Transferrin saturation	Soluble transferrin receptor
IDA	↓	↓	↑	↓	↑
AI	↑/Normal	↓	↓	↓	↓/Normal

Questions:

1) A 32 year old man was found to have a Hb of 7.8 gm/dL with reticulocyte count of 0.8%. B. film showed microcytic hypochromic anaemia. Hb A2 and Hb F levels were 2.4% and 1.3% respectively. Serum iron and TIBC were 15 mgm/dL and 420 mgm/dL respectively. The likely diagnosis is:
    1) a. IDA
    2) b. β thalassemia minor
    3) c. Sideroblastic anaemia
    4) d. Anaemia of chronic inflammation
2) Which of the following test is best in differentiating between anaemia of chronic inflammation and IDA?
    1) a. Serum ferritin
    2) b. Serum transferrin receptor
    3) c. TIBC
    4) d. Transferrin saturation

Thank you