



# HEMATOPOIETIC & LYMPHATIC SYSTEM

-NACHAT BATCH-

SUBJECT : Pharmacology

LEC NO. : 1

DONE BY : Jana Alqhaiwi

وَقُلْ رَبِّ زِدْنِي عِلْمًا

# HEMATOPOIETIC & LYMPHATIC SYSTEM PHARMACOLOGY

## DRUG THERAPY OF ANEMIAS

- Anemia is defined as a low hemoglobin (Hb) concentration due to reduced production or increased loss of RBC. The WHO defines anemia as Hb <13 g/dL in men or <12 g/dL in women.

### Types of anemia:

#### 1. Deficiency Anemia: نقص بالعناصر

مواد خام بتساعد بتصنيع Hb و عناصر مفيدة للتصنيع

يساعد بعملية  
hematopoiesis in  
bone marrow

- Normal erythropoiesis requires certain exogenous substances (iron, folic acid & vitamin B<sub>12</sub>) & some endogenous factors (intrinsic factor, erythropoietin & colony stimulating factors).

يساعد على امتصاص B12

Stimulate bone marrow to produce RBC

- Iron deficiency anemia: due to iron deficiency
- Megaloblastic anemia: due to vitamin B<sub>12</sub>, intrinsic factor, or folic acid deficiency.

#### 2. Aplastic anemia: due to damage of bone marrow

المصنع غير قادر على التصنيع (aplastic anemia)  
Because of tumor, or exposed to radiation

#### 3. Hemolytic anemia: due to destruction of red cells

Rapid rate of destruction of RBC due to drugs or autoimmune disease which produces antibodies to attack RBC and cause hemolysis

## DRUG THERAPY OF IRON-DEFICIENCY ANEMIA

اصغر من الحجم الطبيعي

↓ Hb concentration

### (Microcytic Hypochromic Anemia)

RBC's size and membrane depend on the concentration of Hb

## IRON

### Iron Absorption

- Iron intake occurs from plant-derived foods, in the form of non-heme iron (Fe<sup>3+</sup>, ferric), and from animal-derived foods, in the form of heme iron (Fe<sup>2+</sup>, ferrous)
- Absorption occurs in the duodenum and in the first portion of the jejunum (acid medium ↑ solubility).
- Fe<sup>2+</sup> is directly taken up into the enterocyte (by the heme transporter)

From animal source

## HLS Pharmacology

- $Fe^{3+}$  duodenal cytochrome-B (Dcytb)/cytochrome-b reductase-1  $\rightarrow Fe^{2+}$  which is taken up into the enterocyte (via divalent iron metal transporter-1; DMT1)

Iron ما بضل free لازم يرتبط بapoferritin  
Once ferrous enter the blood, it is oxidized by haphaestin to produce ferric

- $Fe^{2+} + \text{apoferritin} \rightarrow \text{ferritin}$  (the cellular store of iron), so saturation of apoferritin will limit further absorption (mucosal block)

يمكن يصير shedding of duodenum mucosa و ينزل في GIT عن طريق stool للتخلص من iron الزيادة  
Iron cause damage and there is no role of excretion of iron  
Just in this way iron is excreted

### Factors Enhancing Iron Absorption

1. Infancy, adolescence and in iron-deficiency anemia ( $\uparrow$  demand)
2. Ascorbic acid, HCl & succinic acid  $\rightarrow \uparrow$  absorption (ferric  $\rightarrow$  ferrous).

في الحالات الطبيعية يتم امتصاص 10% من كمية iron التي اتاخذت في اليوم لكن في هذه الحالات تزيد عن 25%

### Factors Reducing Iron Absorption

1. Gastric resection and malabsorption syndrome.

2. Desferrioxamine (chelates iron). toxicity  $\rightarrow$  علاج يعمل مع iron مع عشان يصير له excretion in kidney  $\rightarrow$  عكس الحديد

3. Antacids. peptic ulcer, acidity في الفؤارات المستخدمة في

4. Tannic acid (precipitates iron). iron مع complex يعمل في الشاي

5. Ca in dairy food  $\rightarrow \downarrow$  iron absorption

5. Tetracyclines & iron bind together  $\rightarrow \downarrow$  absorption of both.

6. Phosphates & oxalates (form insoluble iron complexes).

in vegetables in tomato

[N.B. Foods that decrease non-heme iron absorption have little effect on absorption of heme iron.]

### Iron Transport:

From plant source

- By the ferroportin transporter,  $Fe^{2+}$  is carried from the enterocyte into the blood stream

- $Fe^{2+}$  is re-oxidized by the enzyme hephaestin in mucosal cells  $\rightarrow Fe^{3+}$

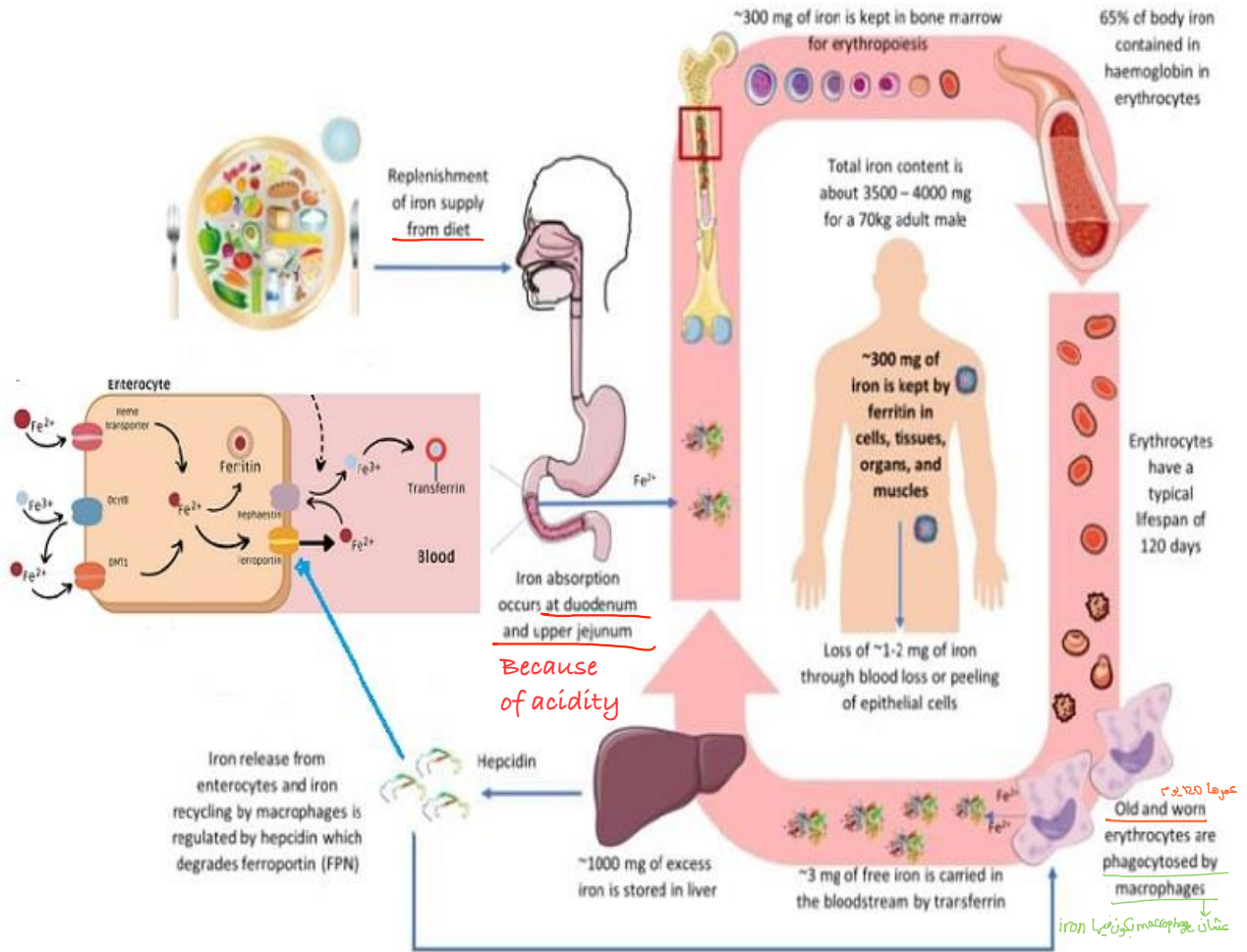
- $Fe^{3+}$  is transported in blood as transferrin to all other tissues in the body and stored in the liver, reticuloendothelial system and bone marrow as ferritin.

Free iron

- Heparidin (a protein synthesized by the liver) regulates iron release from enterocytes and iron recycling by macrophages, and it may contribute to the

anemia of chronic diseases.  $\rightarrow$  When old RBC is phagocytosed by macrophage, iron returns to blood as transferrin. Heparidin is secreted by liver to control ferroportin for decreasing absorption and making macrophage not to release iron because of enough store

مميزة oral preparation  
انه اي اشي يتاخذ oral في control يعني ياخذ اللي محتاجه عكس IM لما وصل blood ما رح يقدر يخرج تاني



## Indications of Iron Therapy

1- Prophylactic of the occurrence of iron-deficiency anemia (IDA):

**30-60 mg/day elemental iron**

2- Treatment of IDA: **200-400 mg/d elemental iron** in 2-3 divided doses/d

*قراءة* (Elemental iron is the total amount of iron in the supplement available for absorption. In Fe deficient individuals, about 50-100 mg of Fe can be incorporated into hemoglobin daily, and about 25% of oral Fe given can be absorbed).

**Iron-Deficiency Anemia due to: (Treatment of the cause is essential).**

1. ↑ **Demand**: premature infants, children, pregnant and lactating women. *غير هذول يكون decrease لل demand*

2. ↓ **Absorption**: after gastrectomy & in malabsorption syndrome.

3. **Chronic blood loss**: e.g., occult GIT bleeding, heavy menstrual bleeding, during hemodialysis, ancylostomiasis. *Helminth بتعيش في GIT و بتعمل sucking للجدار و هذا يؤدي الى bleeding*

4. ↑ **in blood formation**: during treatment of severe pernicious anemia with

① vitamin B<sub>12</sub> (depletion of iron stores)/ ② during treatment with erythropoietin *في حالات renal failure*

*ما في B12 بصيرله absorption بالتالي بصير في erythropoiesis و ما راح يتكون RBC*

*بخلي المصنع يصنع بسرعة RBC و هذا synthesis يحتاج iron*

*So B12, erythropoietin should be taken with iron to avoid iron deficiency anemia*

## Iron Therapy (Oral – Parenteral (IV, IM))

### I. Oral Iron Therapy

لحتى المريض يقدر يتحمل مدة اللي رح ياخذ فيها الدواء لازم تكون adverse effect قليلة

- Effective & cheap (treatment of choice).
- Oral preparations include **ferrous sulfate, gluconate and fumarate**.
- Given after meals to decrease GIT disturbances.
- **New agents: polysaccharide-iron complex, carbonyl iron.** **Heme iron polypeptide:** More expensive.
- Different Fe salts provide different amounts of elemental Fe:

عملوها بطريقة معينة عشان iron → يصيرله امتصاص بشكل بطيء على مدار اليوم عشان يقلل من adverse effect و تعطينا الجرعة اللي انا محتاجها شبه sustained-released

الفرق بينهم في نسبة الحديد الصافي

Iron formulation	ferrous gluconate	ferrous sulfate	ferrous fumarate	polysaccharide-iron complex	Carbonyl iron
Elemental iron	12%	20%	33%	100%	100%

Elemental iron → ↑disturbance to GIT (Adverse effect) والفكس صريح

- Continue iron till Hb is normal (1-2 months) & for an extra 2-4 months to replenish stores.

هل ينفع اوقف العلاج؟ طبعاً لا عشان ما في iron store  
الحل: محتاج لشهرين - 4 شهور اعطي زيادة عشان املا store الموجود في الجسم

Iron salts are usually used as ferrous iron is efficiently absorbed.

### Adverse Effects of Oral Iron Therapy

1. GIT disturbances: nausea, epigastric pain, constipation (given after meals) - start with small dose then gradually increase).  
Empty stomach → ↑absorption → adverse effect  
↓absorption  
لحتى يتعود GIT
2. Black stools (mask diagnosis of GI bleeding).
3. Black staining of teeth (iron sulfide in mouth).

### II. Parenteral Iron Therapy

#### Indications (= Causes of failure of oral iron therapy)

1. Noncompliance to oral therapy (severe GIT disturbance or ulceration).
2. Malabsorption syndrome causes failure of iron absorption.
3. Severe anemia, e.g. in malignancy.

4. Giving erythropoietin to renal failure patients  
حكى الدكتور اكتوبها وعادها اكثر من مرة بالمحاضرة

