SAWA UNIVERSITY

امراض الدم الكورس الأول

Iron deficiency anemia

Sawa University — جامعـــــة ســـــــاوة الاهلية

College of health and medical techniques — كليـــــة التقنيـــات الصحيـة والطبيـة

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. ..... Third ..... Stage — ....المرحلـــــــــــــة .....الثالثة

محاضرة رقم 6

Lecture No. 6

الجانب النظري

Theoretical

تدريسي المادة : د وضاح علي حسين

CONTENTS OF THIS TEMPLATE

- Iron metabolism
- Iron deficiency anemia

Iron deficiency anemia

Anemia Definition : Reduced oxygen carrying capacity of blood

Reduction in the hemoglobin conc. of blood •

Reduction in the volume of packed red cells • (Hematocrit)

Reduction of the total circulating red cell mass • below normal limits

WHO criteria is Hg < 13 in men and Hg < 12 in women

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Morphological Classification of Anemia

Based on Red cell size, degree of hemoglobinization & Red cell indices

Normochromic anemia

MCV, MCH, MCHC are normal **(MCV 80-97FL**)

eg: Acute blood loss, Hemolytic anemias, Aplastic anemia, Anemia of chronic disorder

Microcytic hypochromic anemia

MCV less than 80fl , MCH , MCHC all are decreased

Macrocytic normochromic anemia

MCV , MCH increased ; MCHC normal eg: Megaloblastic anemia, **(MCV > 100 FL**)
Liver disorders, MDS

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Pathophysiologic Classification of Anemias

I. Blood loss

: II. Impaired Red cell Production

III. Increased Rate of destruction : (Hemolytic anemia)

I. Blood loss

i) Acute : Trauma

.ii) Chronic : Lesions of GIT / Gynecologic disturbances (Menorrhagia) etc

.

: II. Impaired Red cell Production

Disturbance of Proliferation & differentiation of stem cells : Aplastic anemia, pure red cell (1 aplasia, Anemia of renal failure

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Disturbance of proliferation & maturation of erythroblasts (2

a . Defective DNA Synthesis : Megaloblastic anemia

: b. Defective hemoglobin Synthesis

Deficient heme Synthesis : Iron deficiency

Deficient globin Synthesis : Thalassemias

: c. Multiple mechanisms

Sideroblastic anemia, Myelophthisic anemias due to marrow infiltrations, Anemia of chronic infections

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III. Increased Rate of destruction : (Hemolytic anemia)

Intrinsic (Intra corpuscular) abnormalities of red cells **

Hereditary (.1

Red cell membrane disorders :Hereditary Spherocytosis •

Red cell enzyme deficiencies : G6 PD deficiency •

Structurally abnormal globin synthesis : Sickle cell anemia •

: Acquired (.2

Membrane defect : Paroxysmal nocturnal hemoglobinuria (PNH)

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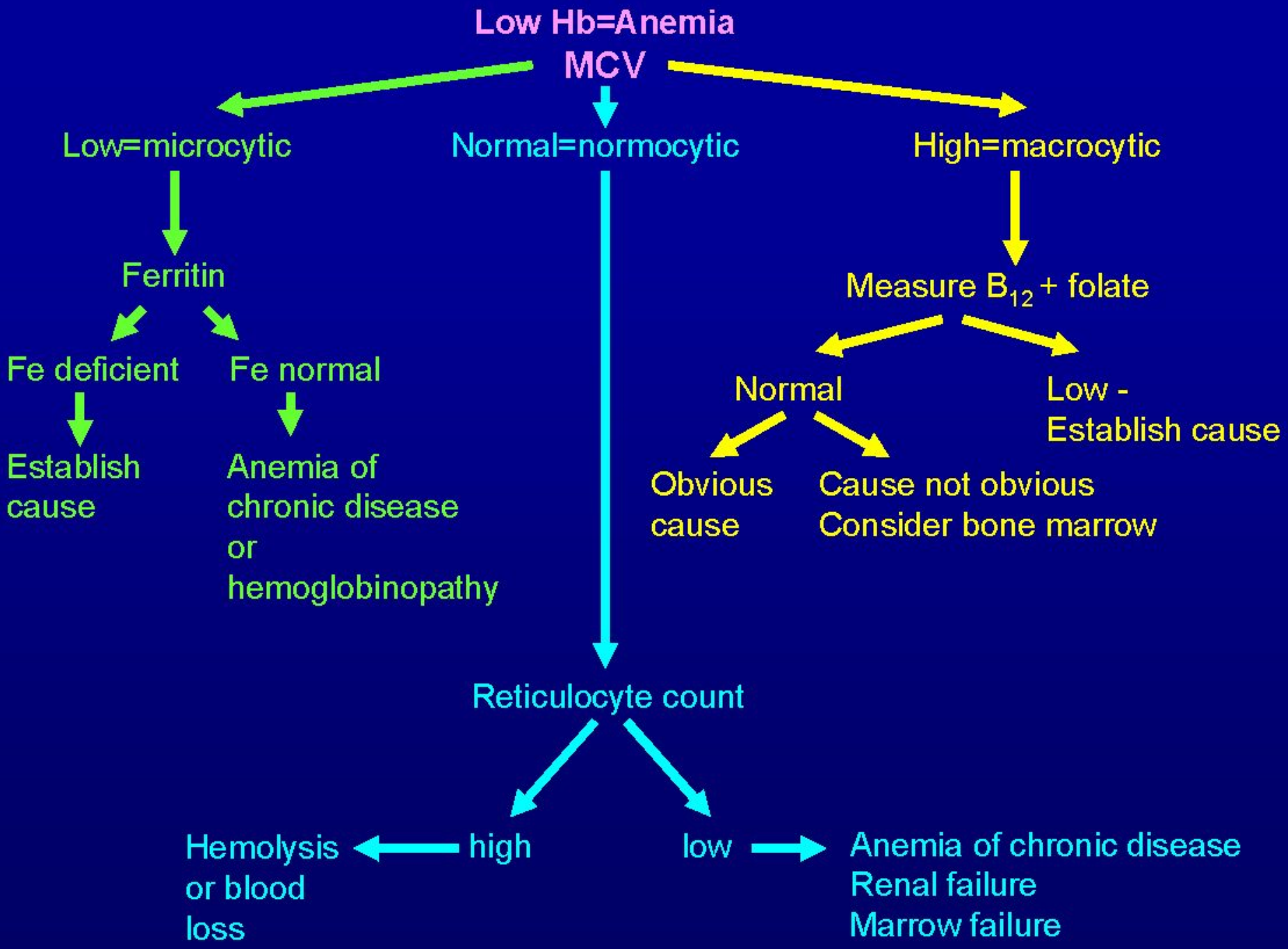
:Extrinsic (Extra corpuscular) abnormalities

1. Antibody mediated : a)alloantibodies : Transfusion reactions
,b) Autoantibodies : Idiopathic, SLE, Drug induced malignant neoplasms
2. Mechanical trauma to red cells : Microangiopathic hemolytic anemia (MAHA), TTP,DIC
3. (Infections : Malaria, Hookworm infestation
4. Chemical injury : Lead poisoning


Low Hb=Anemia
MCV
Low=microcytic
Normal=normocytic
High=macrocytic
Ferritin
Fe deficient
Fe normal
Establish cause
Anemia of chronic disease or hemoglobinopathy
Measure B_{12} + folate
Normal
Low - Establish cause
Obvious cause
Cause not obvious Consider bone marrow
Reticulocyte count
high
low
Hemolysis or blood loss
Anemia of chronic disease
Renal failure
Marrow failure

Iron deficiency anemia

. Most common nutritional disorder in the world IDA

Iron in the body used for the synthesis of Hemoglobin and normal

.erythropoiesis requires 20-25 mg of iron per day

Total body Iron content in •

Men : 4 – 6 gm

Women : 2 – 4 gm

: Functional Iron (Two third)•

; Hemoglobin (80%)

;Myoglobin (3.5%)

Iron-Containing enzymes-catalase & cytochromes (0.5%)

Storage Iron (one third) : Ferritin & Hemosiderin •

Storage iron

Ferritin : Protein-Iron complex found in all tissues particularly in liver, spleen, BM & skeletal muscles

In liver stored in parenchymal cells •

In spleen & BM (RES) in mononuclear phagocytic cells •

Hemosiderin : Formed by partial digestion of ferritin by lysosomal enzymes

Normally : Only trace amounts are found in body mainly in mononuclear phagocytic cells in BM, spleen & liver

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DISTRIBUTION OF IRON IN NORMAL ADULTS

Functional compounds	
hemoglobin	2,230 mg
myoglobin	140 mg
tissue enzymes	8 mg
Transport	
transferrin	4 mg
Stores (ferritin, hemosiderin)	
males	1000-1400 mg
females	200-400 mg

Iron metabolism *

:Dietary Iron •

..Iron is essential element and must be precisely regulated

Iron absorption is regulated by Hepcidin, a small circulating peptide synthesized & released from liver

Hepcidin inhibits iron uptake in the duodenum & iron release from macrophages •

On the lumen side of small intestine iron is reduced from its ferric form(Fe^{3+}) to• ferrous form(Fe^{2+})

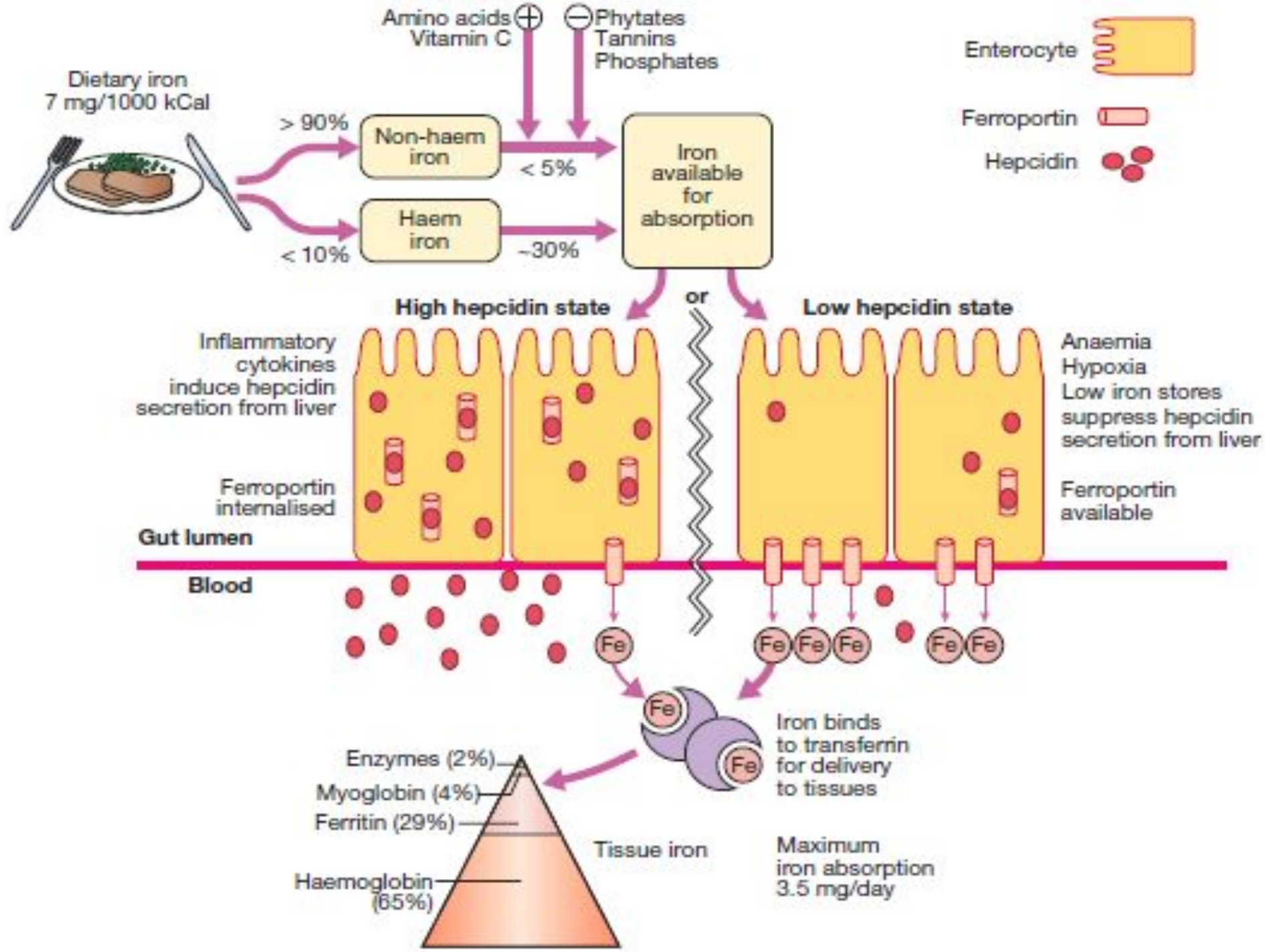
Ferrous iron is then transported in enterocytes by DMT1(divalent metal transporter)

Iron can be either stored within the enterocyte as ferritin or it can be transferred

across the basolateral membrane to the plasma by transport protein

.FERROPORTIN1

.


Amino acids
Vitamin C
Phytates
Tannins
Phosphates
Enterocyte
Ferroportin
Hepcidin
Dietary iron
7 mg/1000 kCal
> 90%
Non-haem iron
< 5%
Iron available for absorption
Haem iron
< 10%
~30%
High hepcidin state
or
Low hepcidin state
Inflammatory cytokines induce hepcidin secretion from liver
Anaemia
Hypoxia
Low iron stores suppress hepcidin secretion from liver
Ferroportin internalised
Ferroportin available
Gut lumen
Blood
Fe
Iron binds to transferrin for delivery to tissues
Enzymes (2%)
Myoglobin (4%)
Ferritin (29%)
Haemoglobin (65%)
Tissue iron
Maximum iron absorption 3.5 mg/day

TRANSPORT PROTEINS

DMT1 (Divalent Metal Transporter 1) .1

Transports from lumen into the enterocytes

FERROPORTIN1 *export protein* .2

Transports from inside enterocytes to circulation

Transferrin *transport protein* .3

carry iron in the blood to RBC precursors in the bone marrow

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Bio availability of Iron

Daily Iron requirement for adult •

Men : 7 to 10 mg adult

Women : 7 to 20 mg

Average daily intake of Iron : 10 to 20 mg •

: Bioavailability of Dietary Iron

Heme Iron is more absorbable than inorganic Iron •

: Increase Absorption of Inorganic Iron •

Ascorbic acid, citric acid, amino acids & Sugars in the diet

: Decrease Absorption •

,Tannates (Tea), Carbonates(cool drinks), Oxalates ,Calcium Phosphates & Phytates (Legumes)

Iron absorption*

Maximum absorption in duodenum and upper jejunum.

The acidic gastric juice reduces insoluble ferric iron to its soluble ferrous state.

: Iron in food •

Heme Iron

(Animal Products: Red meat, Fish & Poultry)

Non Heme Iron

(Inorganic Iron: gree vegetables,Lentils,Beans &Raisins)

Both enter a common pool in mucosal cells & stored as ferritin •

.Transferrin is a transport protein with two iron binding site

transferrin picks up iron from the mucosal cells of the intestine then . deliver iron to receptors on surface of nucleated RBCs and reticulocytes

The amount of transferrin in the serum is measured directly as the total . .iron binding capacity(TIBC)

????QUESTION

Regulation of iron uptake and storage

Who is playing the central role in IRON ??METABOLISM

ANSWER

HEPCIDIN is the key regulator of iron in our .body

??What is HEPICIDIN

Is a peptide hormone produced in the liver which was first identified in human urine and plasma in .2000

.Its molecular weight is 25 Kda

.Highly folded structure

Present in inactive form;prohepcidin(60aa) and its .active form is hepicidin(25aa)

*

.

Hepcidin is a key regulator of iron release from villus .enterocytes and macrophages

Hepcidin, whose production is upregulated by high plasma iron levels or inflammation, inhibits iron release .from these cells and lowers GI absorption

Low iron levels decrease hepcidin production, which in turn stimulates iron absorption and release into the blood

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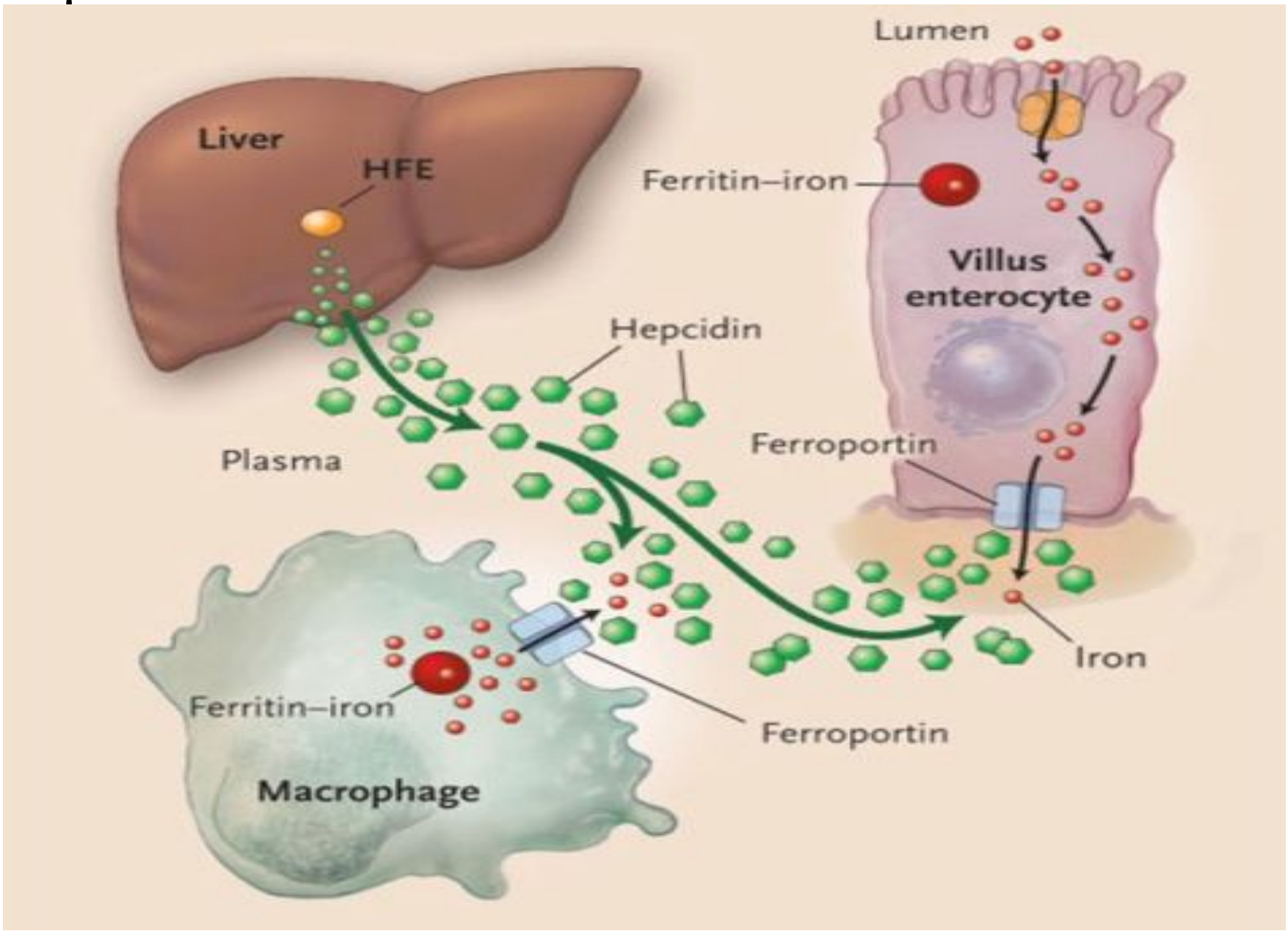
Lumen
Liver
HFE
Ferritin–iron
Villus enterocyte
Hepcidin
Plasma
Ferroportin
Iron
Ferritin–iron
Ferroportin
Macrophage

*

Plasma levels of iron are closely regulated to ensure a daily supply of about 20 mg to the bone marrow for incorporation into .hemoglobin

Most of the iron in the plasma derives from the continuous .breakdown of hemoglobin in senescent red cells by macrophages

to 2 mg per day of iron is also taken up by duodenal enterocytes 1 and transferred to the plasma compartment or, depending on .body needs, stored in the enterocytes as ferritin

.

Iron recycled by macrophages and that absorbed from the gut is loaded on to serum transferrin and delivered primarily to the bone .marrow for reincorporation into new red-cell precursors

The remaining body iron (about 1000 mg) is stored, primarily in .hepatocytes

*

the total body iron in a 70-kg man is about 4 g. This is maintained by a balance between absorption and body .losses

Although the body only absorbs 1 mg daily to maintain equilibrium, the internal requirement for iron is greater .(20-25 mg)

A man with 5 L of blood volume has 2.5 g of iron incorporated into the hemoglobin, with a daily turnover of 20 mg for hemoglobin synthesis and degradation and .another 5 mg for other requirements

Most of this iron passes through the plasma for reutilization. Iron in excess of these requirements is .deposited in body stores as ferritin or hemosiderin

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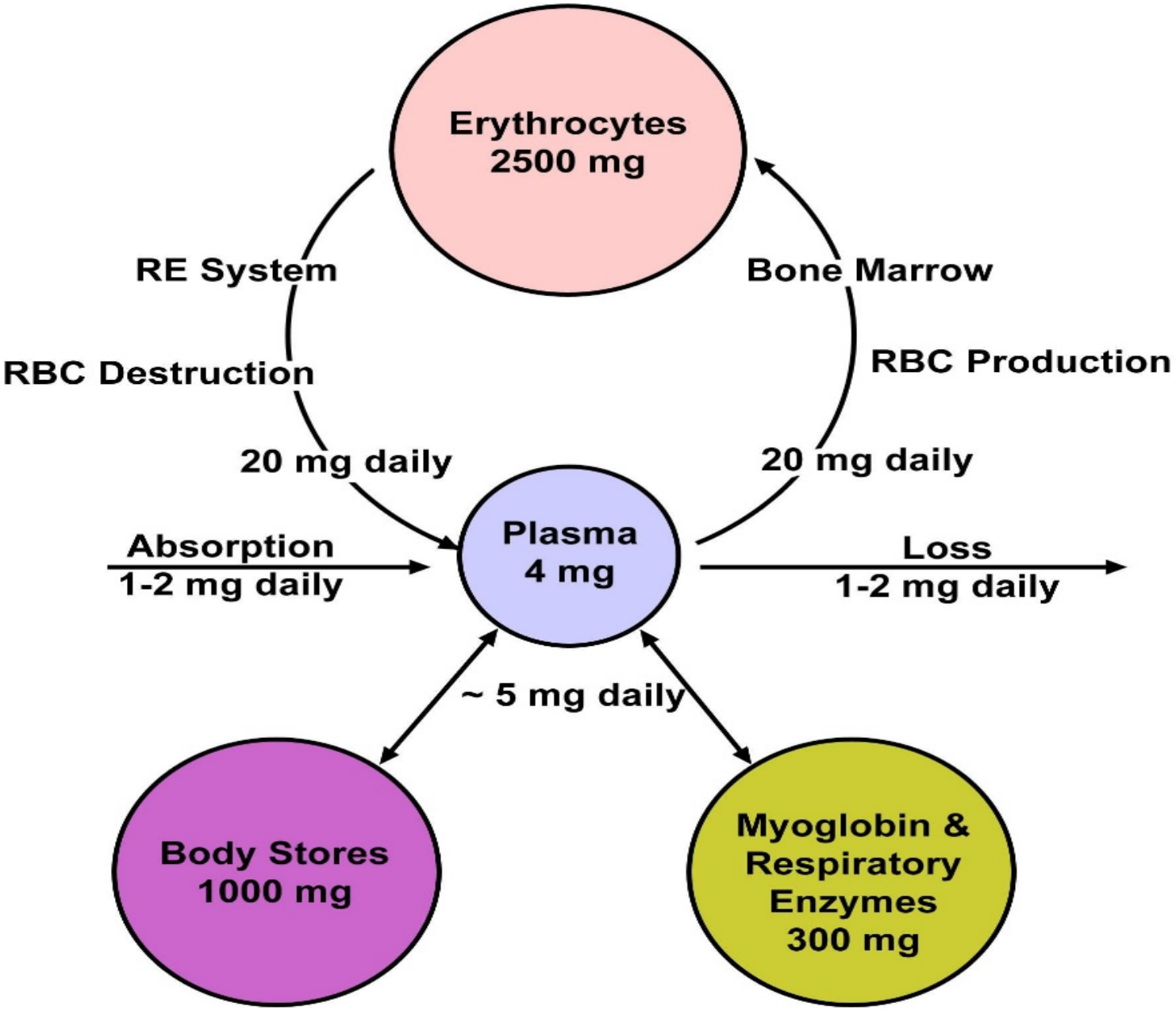

Erythrocytes
2500 mg
RE System
RBC Destruction
20 mg daily
Bone Marrow
RBC Production
20 mg daily
Absorption
1-2 mg daily
Plasma
4 mg
Loss
1-2 mg daily
~ 5 mg daily
Body Stores
1000 mg
Myoglobin &
Respiratory
Enzymes
300 mg

******** Etiology of IDA

: I. Inadequate Dietary intake

Poor economic status .1

Elderly : with restricted diet due to poor dentition / .2 limited income

,.Anorexia :Chronic disorders, Malignancies etc .3

: II. Impaired absorption

Partial or total gastrectomy .1

. Malabsorption syndromes :,**Celiac disease** .2

: III. Increased requirement

Spurts of growth in infancy, childhood & adolescence.1

Pregnancy & lactation .2

*

:IV. Chronic blood loss

Uterine : **Menorrhagia**, Malignancies .1

Gastro intestional : Hookworm infestation (worldwide .2 most common cause) , Peptic ulcers, **hemorrhoids**, **Gastrointestinal malignancies**

long term use of NSAIDS (Aspirin) ,

Urinary tract : Hematuria, Tumors .3

Lung : Hemoptysis .4

Nose : Epistaxis .5

Deficiency in adult men & Post menopausal women must be attributed to GI blood loss until proven otherwise

IDA – Clinical features

Fatigue, Dyspnoea on exertion, palpitations •

Pallor of skin, sclerae & mucous membrane •

Koilonychia, alopecia, atrophic glossitis •

: Plummer vinson syndrome •

Microcytic hypochromic anemia (1

Atrophic glossitis (2

Esophageal webs(3

Stages of development of Anemia

: Storage Iron depletion

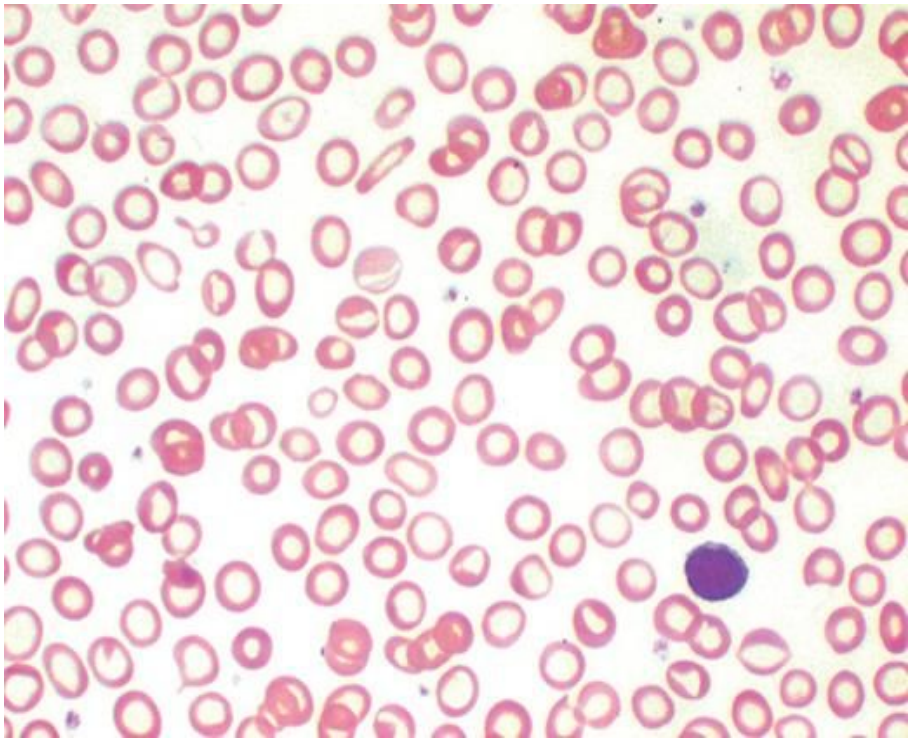
decrease Serum ferritin .1

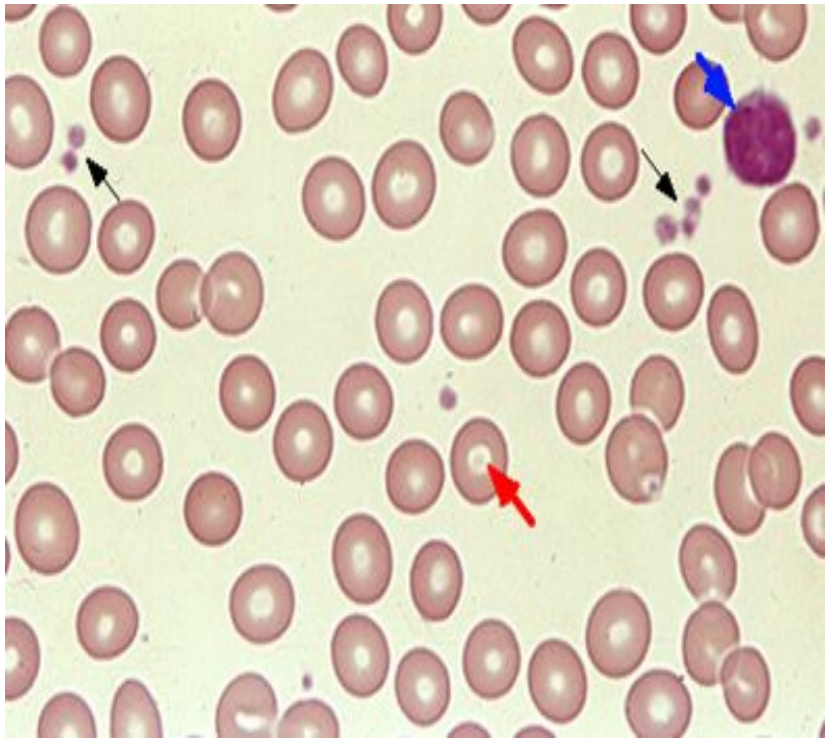
Loss of circulating Iron : Increased erythroid activity in marrow, .2 decrease serum Iron, decrease TIBC

Frank Iron deficiency anemia .3

Physical Manifestation : “Koilonychia” in Iron Deficiency

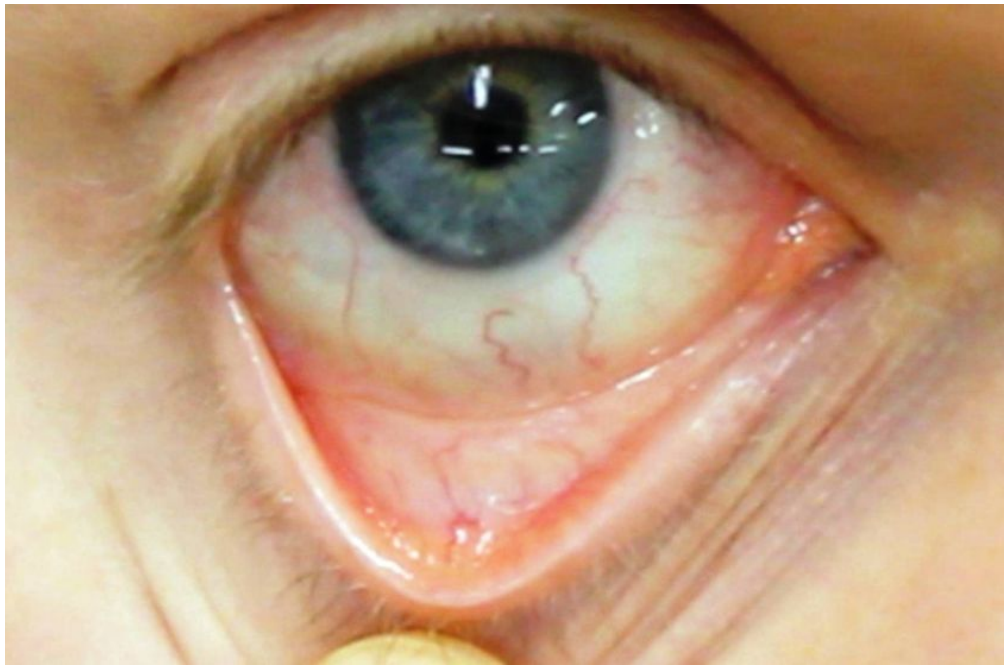
Peripheral blood



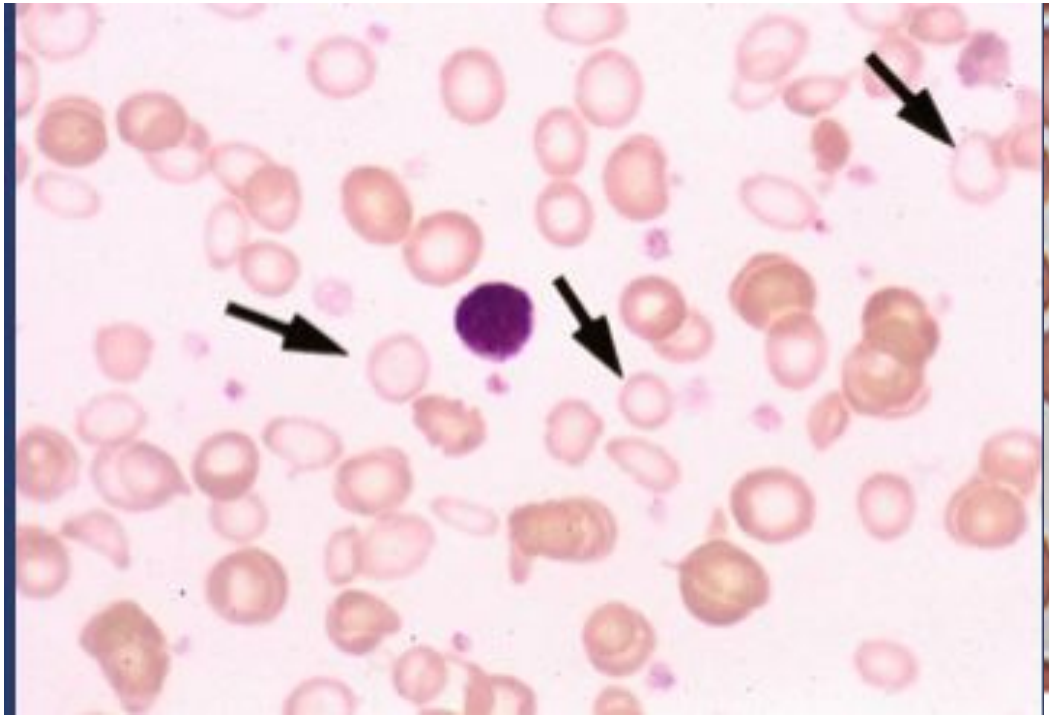


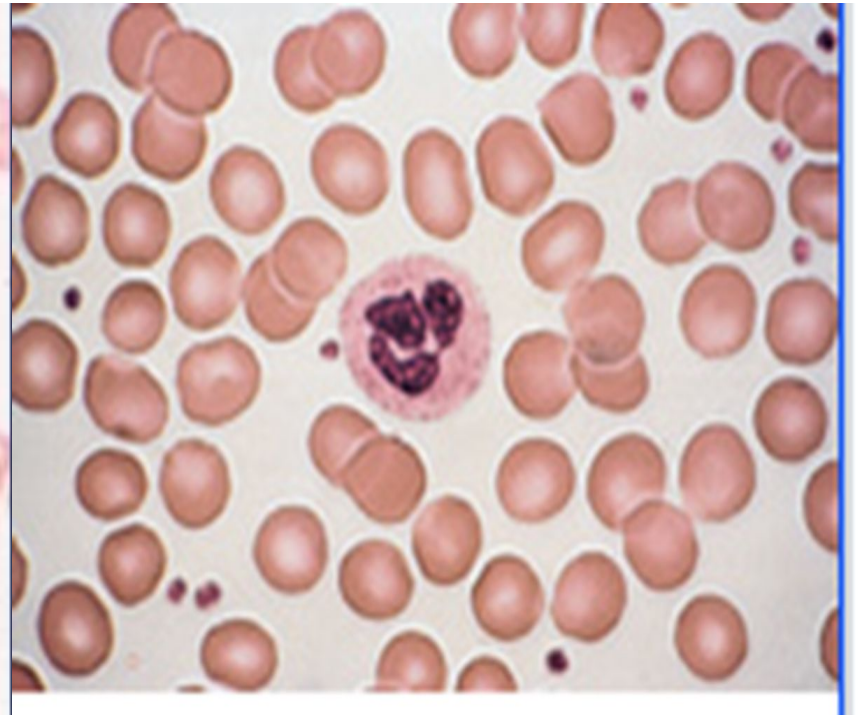
Pallor

Pallor



Iron Deficiency Anemia: Peripheral Smear





– Iron deficiency anemia can cause •

Brittle nails –

Cracks at angle of the mouth –

, Unusual craving for substances like ice, paint –

Pica eating clay –

Some people have restless leg syndrome – strong •

urge to move legs

****

Hypochromic Anemias

Iron deficiency anemia.1

Sideroblastic Anemia.2

Thalassaemia Minor.3

Anemia of Chronic disorders.4

:DIAGNOSIS

- Laboratory studies :
- a. peripheral blood :

1. **RBC indices** :

MCV (55-74 fl)

MCH (25-30 g/dL)

RDW > 16

- 2. **Peripheral blood smears** :

microcytic hypochromic

poikilocyte = abnormally shaped RBCs.

Anisocyte = vary in size of RBCs.

- 3. Blood count :

normal or low reticulocytes

- occasionally high platelet count.

.Investigation-cont

- **b. serum iron studies :**
- the level of serum iron is low or normal depending on what patient eat before the measurement.
- TIBC > 400 µg/dL
- Transferrin saturation <15 %
- Serum Ferritin < 12 ng/ml.
- **Soluble transferrin receptor ; increased**
- **C. Bone marrow studies :**
- Absence of iron in macrophage when the sample is subjected to Perl's stain (Prussian blue stain)

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Laboratory findings in IDA

l. Blood picture & Red cell indices

Hb : Decreased in variable degree.1

R.B.C : - Count is decreased.2

Blood indices : decrease MCV, MCH & MCHC RDW is an .3 early & pronounced finding

Peripheral Smear : Microcytic & Hypochromic R.B.C.4
Poikilocytosis : Target cells, pencil cells & teardrop cells

Laboratory findings in IDA

ll. Bone Marrow findings

Cellularity :increased Due to erythroid hyperplasia .1

Erythropoiesis : Micronormoblasts Cytoplasmic .2 maturation lags behind so that late normoblasts have pyknotic nuclei but persisting polychromatic cytoplasm

Marrow Iron stores.3

Depleted : (Perl's stain with prussian blue reaction)

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Laboratory findings in IDA

III. Biochemical findings

Serum Iron levels – Low (N: 80-180 ug/dl) .1

Total plasma Iron binding capacity (TIBC) High .2

resulting in →(Reflects Transferrin concentration) (N: 250-450 ug/dl)

decrease transferrin saturation < 15%

In Anemias of chronic disorders both serum Iron & TIBC •

are reduced

Serum ferritin levels-Low (N :150-200 ng/dl) .3

Free Erythrocyte protoporphyrin : Elevated due to .4

reduced heme synthesis

TREATMENT

- **1- Determine the cause of iron deficiency.**
- stool for occult blood loss from GIT bleeding.
- radiological analysis of upper & lower GIT for occult malignancy.
- urine analysis for hematuria.
- CXR for pulmonary Hemosiderosis.

Serum anti endomysial antibody antibodies ,tissue transglutaminase

antibodies and possibly a duodenal biopsy are indicated to detect coeliac

. disease

. •

.Treat the underlying cause-2

- **3- Initiate iron replacement therapy :**
- oral iron therapy :
- Ferrous sulfate.
- Ferrous fumarate and gluconate.
- **Dosage :**
- The adult dose of ferrous sulfate is 300 mg/day gradually increased to 900 mg /day if tolerated.
- **Adverse effect :**
- GIT irritation : nausea, cramping, diarrhea.

Indication of iron injection therapy

- can not tolerate the side effect of oral iron.
- Suffers from inflammatory bowel disease and peptic ulcers.
- Does not comply with prescribed dosage.
- Iron mal-absoption.
- Suffers from condition such as hereditary hemorrhagic telengectasis (HHT) in which the rapid loss from continuous bleeding can not be compensated by oral iron.
- Transfusion of whole blood or packed red cells is generally not indicated unless a rapid increase in haematocit is critical to the patient.

Treatment IDA

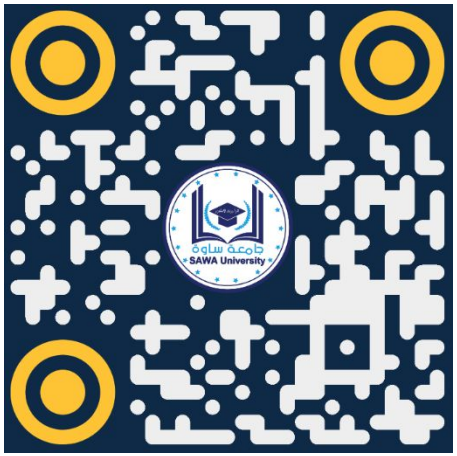
Table 103-5 Oral Iron Preparations		
Generic Name	**Tablet (Iron Content), mg**	**Elixir (Iron Content), mg in 5 mL**
Ferrous sulfate	325 (65) 195 (39)	300 (60) 90 (18)
Extended release	525 (105)	
Ferrous fumarate	325 (107) 195 (64)	 100 (33)
Ferrous gluconate	325 (39)	300 (35)
Polysaccharide iron	150 (150) 50 (50)	100 (100)

Conclusions

- Microcytic, Hypochromic picture
- decrease Serum Iron & Ferritin levels
- increase TIBC Presence of increased storage Iron in marrow macrophages, high serum ferritin levels and reduced TIBC readily rules out Iron deficiency as the cause of anemia

Q1 Morphological Classification of Anemia

Q2 Laboratory finding in iron deficiency anemia



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