Introduction to anemia , classification and strategies for diagnosis.

Sura Al Rawabdeh . MD

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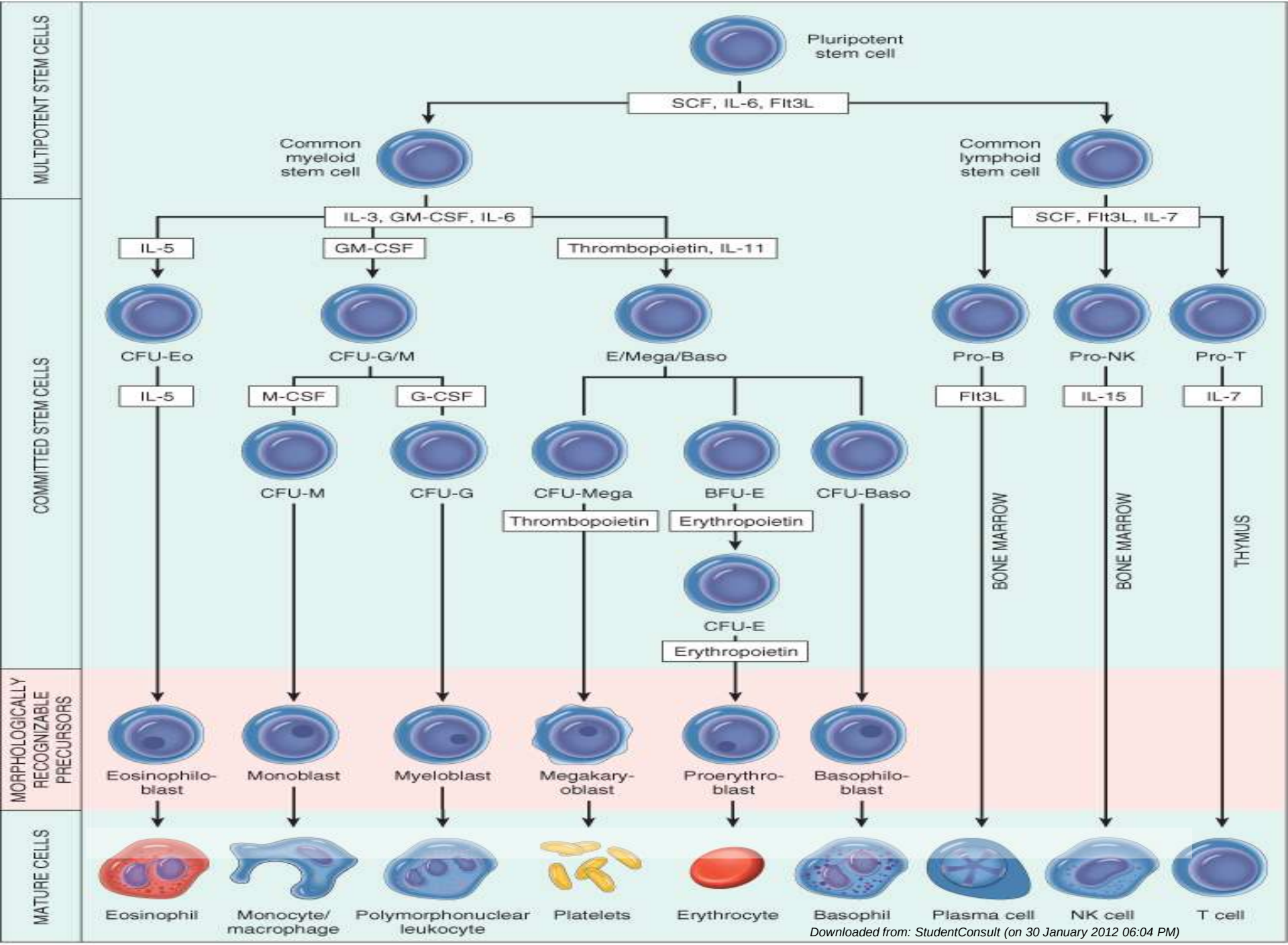


Introduction

- The hematopoietic and lymphoid systems are affected by

a wide spectrum of diseases.

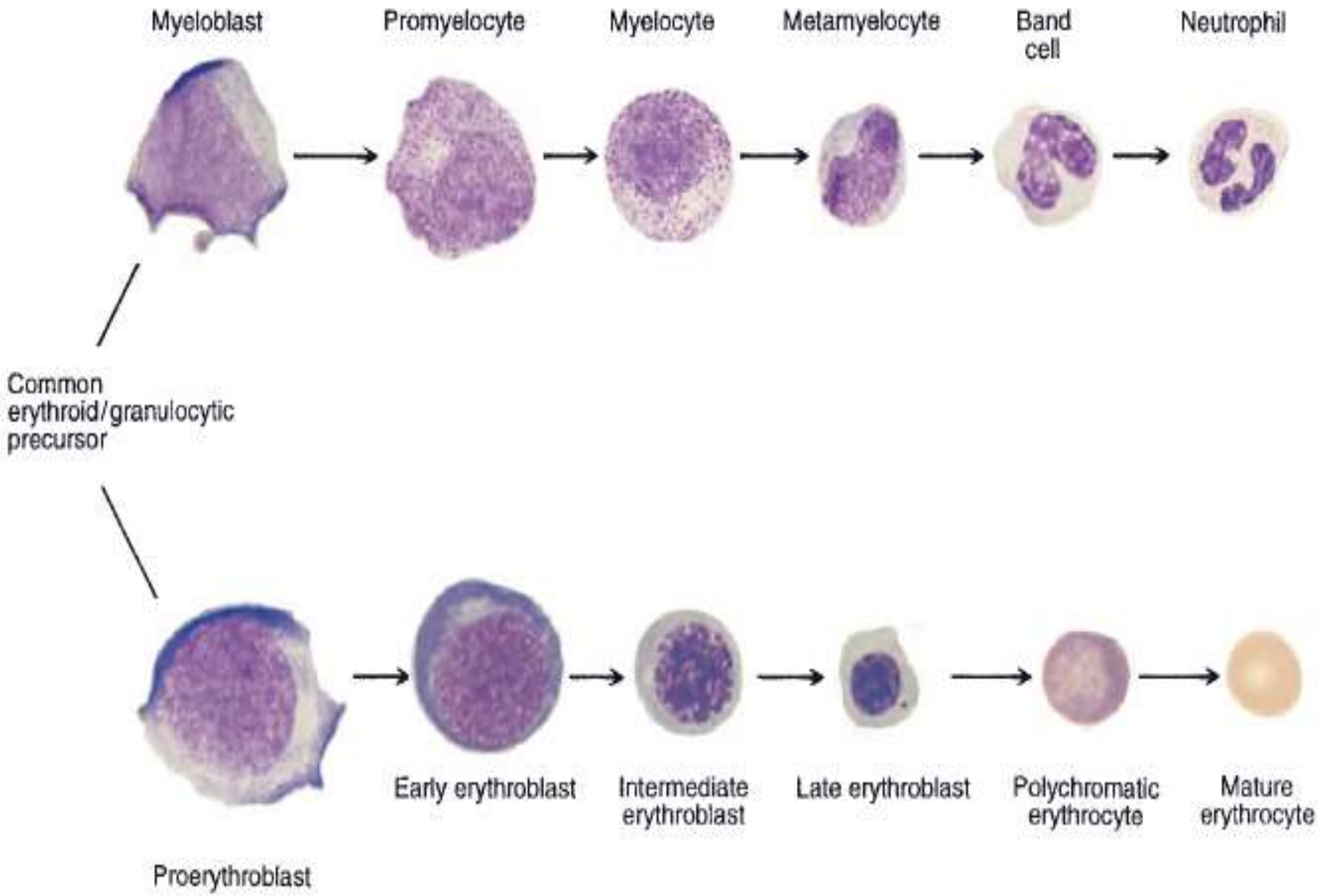
- Classification of hematolymphoid disorders based on Predominant involvement of :

1- red cells

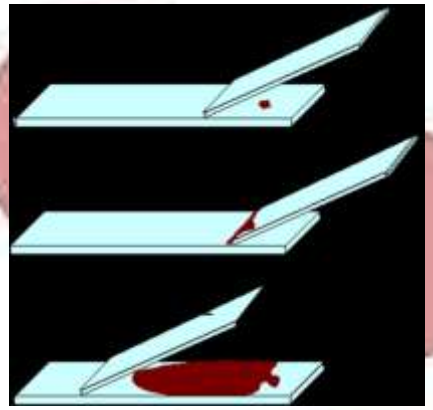
2- white cells

3- the coagulation system, which includes platelets and clotting factors.

- Although these divisions are useful, in reality the production, function, and destruction of red cells, white cells, and components of the hemostatic system are closely linked, and derangements primarily affecting one cell type or component of the system often lead to alterations in others.


Myeloblast
Promyelocyte
Myelocyte
Metamyelocyte
Band cell
Neutrophil
Common erythroid/granulocytic precursor
Early erythroblast
Intermediate erythroblast
Late erythroblast
Polychromatic erythrocyte
Mature erythrocyte
Proerythroblast

Smear of peripheral blood



erythrocyte

lymphocyte

neutrophil

eosinophil

basophil

monocyte

Complete Blood Count (CBC)

The CBC offers a quantitative assessment of each of the blood's cellular elements.

Classification on the basis of red cell morphology

- **Hemoglobin (HGB):** (g/dl)

- **Mean cell volume (MCV):** the average volume per red cell, expressed in femtoliters (cubic microns). Hematocrit/ RBCs count.(**fl)**

- **Mean cell hemoglobin (MCH):** the average mass of hemoglobin per red cell, expressed in picograms. Hemoglobin / RBCs count.

- **Mean cell hemoglobin concentration (MCHC):** the average concentration of hemoglobin in a given volume of packed red cells, expressed in grams per deciliter. Measures concentration of Hb in a given volume of packed RBCs.

Hemoglobin (g/dl) / Hematocrit .

- **Red cell distribution width (RDW):** the coefficient of variation

of red cell volume

- **Packed Cell Volume (PCV):** The ratio of the volume of red cells to the volume of whole blood [%]

Adult Reference Ranges for Red Blood Cells[a]

	Units	Men	Women
Hemoglobin (Hb)	g/dL	13.2–16.7	11.9–15.0
Hematocrit (Hct)	%	38–48	35–44
Red cell count	$\times 10^6/\mu L$	4.2–5.6	3.8–5.0
Reticulocyte count	%	0.5–1.5	0.5–1.5
Mean cell volume (MCV)	fL	81–97	81–97
Mean cell Hb (MCH)	pg	28–34	28–34
Mean cell Hb concentration (MCHC)	g/dL	33–35	33–35
Red cell distribution width (RDW)		11.5–14.8	

[a]Reference ranges vary among laboratories. The reference ranges for the laboratory providing the result should always be used in interpreting a laboratory test.

Table 1. Age-Related Variations in Hemoglobin Level and MCV

	Hemoglobin level (g per dL [g per L])		*MCV (μm^3 [fL])*	
Age	*Mean*	*Diagnostic of anemia*	*Mean*	*Diagnostic of microcytosis*
3 to 6 months	11.5 (115)	9.5 (95)	91 (91)	74 (74)
6 months to 2 years	12.0 (120)	10.5 (105)	78 (78)	70 (70)
2 to 6 years	12.5 (125)	11.5 (115)	81 (81)	75 (75)
6 to 12 years	13.5 (135)	11.5 (115)	86 (86)	77 (77)
12 to 18 years (female)	14.0 (140)	12.0 (120)	90 (90)	78 (78)
12 to 18 years (male)	14.5 (145)	13.0 (130)	88 (88)	78 (78)
20 to 59 years (white men)	NA	13.7 (137)	90 (90)	80 (80)
60 years and older (white men)	NA	13.2 (132)	90	80
20 years and older (white women)	NA	12.2 (122)	90	80
20 to 59 years (black men)	NA	12.9 (129)	90	80
60 years and older (black men)	NA	12.7 (127)	90	80
20 years and older (black women)	NA	11.5 (115)	90	80

MCV = mean corpuscular volume; NA = not available.

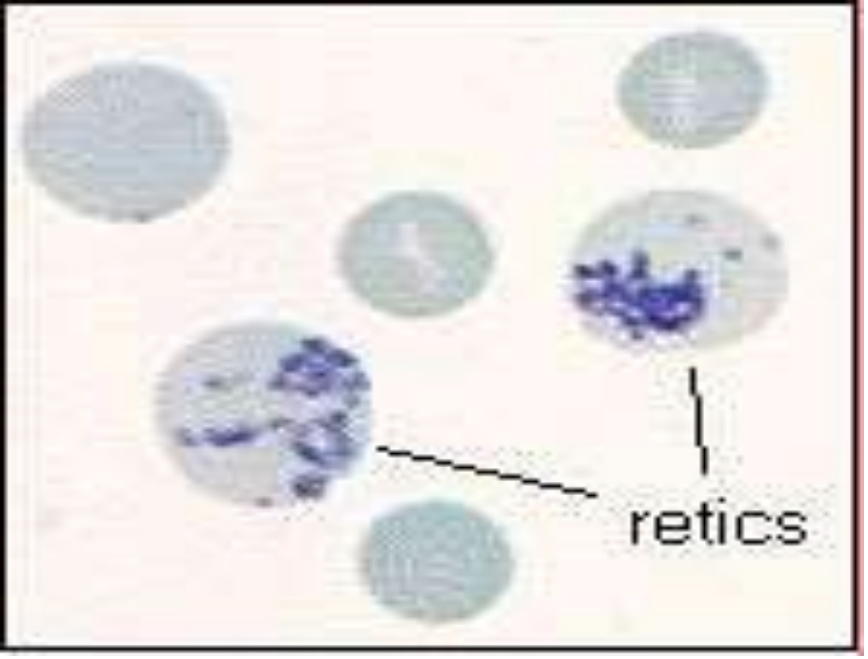
Adapted with permission from Van Vranken M. Evaluation of microcytosis. Am Fam Physician. *2010;82(9):1118.*

CBC.normal reference values.part one

	adults	children
WBC (K/ul)	4-11	4-13
PMN	50-70% [2500-7500/mm^3]	1200-7000/mm^3
BAND	2-6% [100-700/mm^3]	<1000/mm^3
LYMPH	20-45% [950-4500/mm^3]	1500-6000/mm^3
MONO	2-9% [100-950/mm^3]	<1000/mm^3
EOS	0-4% [0-450/mm^3]	<700/mm^3
BASO	0-2% [0-200/mm^3]	<200/mm^3

Reticulocyte Count

- A reticulocyte is a newly released RBC (<36 hours), it contains residual RNA.
- Normal reticulocyte count is less than 1.5%.
- In anemia, one should correct the % of reticulocytes.
- Corrected reticulocyte count= Retic. count x Hct/45.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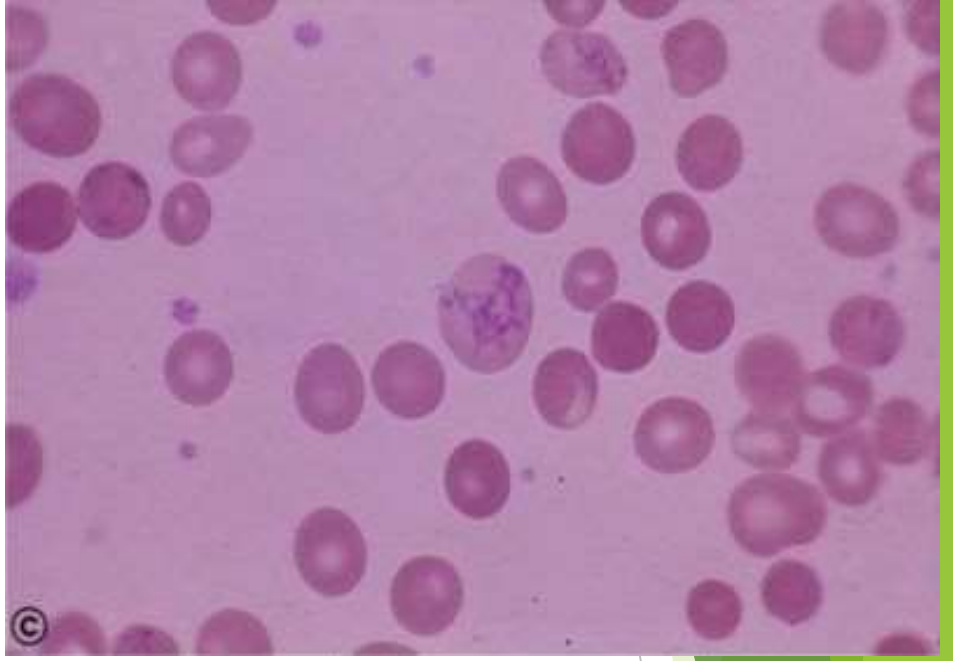
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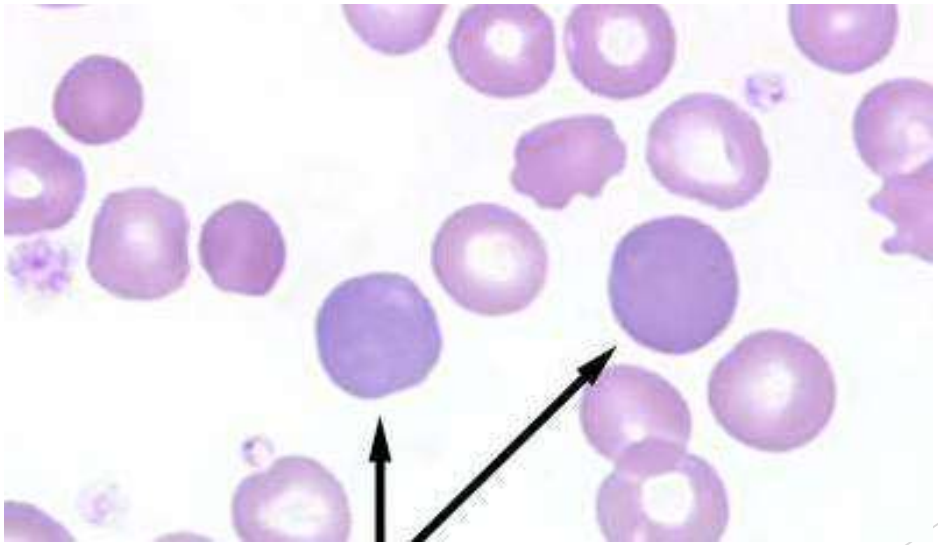


Red Cell Disorders

- Disorders of red cells can result in anemia or, less commonly, polycythemia (an increase in red cells also known as erythrocytosis).

- Anemia is defined as a reduction in the oxygen-transporting capacity of blood, resulting from a decrease in the red cell mass to subnormal levels.

- **Anemia can stem from bleeding, increased red cell destruction, or decreased red cell production.**

- Anemia also can be classified on the basis of red cell morphology. Features that provide etiologic clues include the size, color, and shape of the red cells.

- the clinical consequences of anemia are determined by its severity, rapidity of onset, and underlying pathogenic mechanism.

- The decrease in tissue oxygen tension that accompanies anemia triggers increased production of the growth factor erythropoietin from specialized cells in the kidney →

a compensatory hyperplasia of erythroid precursors in the bone marrow and, in severe anemia, the appearance of extramedullary hematopoiesis within the secondary hematopoietic organs.

- The rise in marrow output is signaled by the appearance of increased numbers of newly formed red cells (reticulocytes) in the peripheral blood. By contrast, anemia caused by decreased red cell production
- (a regenerative anemia) is associated with subnormal reticulocyte counts (reticulocytopenia).

Anemia

Definition

- Hb<13 g/dl (male)
- Hb<12 g/dl (female)

- Anemia is not a diagnosis but a sign of disease.

Classification of Anemia: *Functional

1. **Blood Loss.**
   - acute
   - chronic

2.i **Hypoproliferative**
   - Marrow aplasia
   - Myelophthisic anemia
   - Anemia of chronic disease
   - Anemia with organ failure

- **Dilutional Anemias**
   - Pregnancy

2.ii **Maturational Defect**
   - Cytoplasmic
   - Nuclear
   - Combined

3. **Hemolytic Anemia**
   - Immune hemolysis
   - Membrane defects
   - Hemoglobinopathies
   - Enzymopathies
   - Toxic hemolysis
   - Traumatic hemolysis
   - Hypersplenism

Classification of Anemia According to Underlying Mechanism

Blood Loss

Acute: trauma
Chronic: gastrointestinal tract lesions, gynecologic disturbances

Increased Destruction (Hemolytic Anemias)

Intrinsic (Intracorpuscular) Abnormalities

Hereditary
Membrane abnormalities
- Membrane skeleton proteins: spherocytosis, elliptocytosis
- Membrane lipids: abetalipoproteinemia

Enzyme deficiencies
- Enzymes of hexose monophosphate shunt: glucose-6-phosphate dehydrogenase, glutathione synthetase
- Glycolytic enzymes: pyruvate kinase, hexokinase

Disorders of hemoglobin synthesis
- Structurally abnormal globin synthesis (hemoglobinopathies): sickle cell anemia, unstable hemoglobins
- Deficient globin synthesis: thalassemia syndromes

Acquired
Membrane defect: paroxysmal nocturnal hemoglobinuria

Extrinsic (Extracorpuscular) Abnormalities

Antibody-mediated
- Isohemagglutinins: transfusion reactions, immune hydrops (Rh disease of the newborn)
- Autoantibodies: idiopathic (primary), drug-associated, systemic lupus erythematosus

Mechanical trauma to red cells
- Microangiopathic hemolytic anemias: thrombotic thrombocytopenic purpura, disseminated intravascular coagulation
- Defective cardiac valves

Infections: malaria

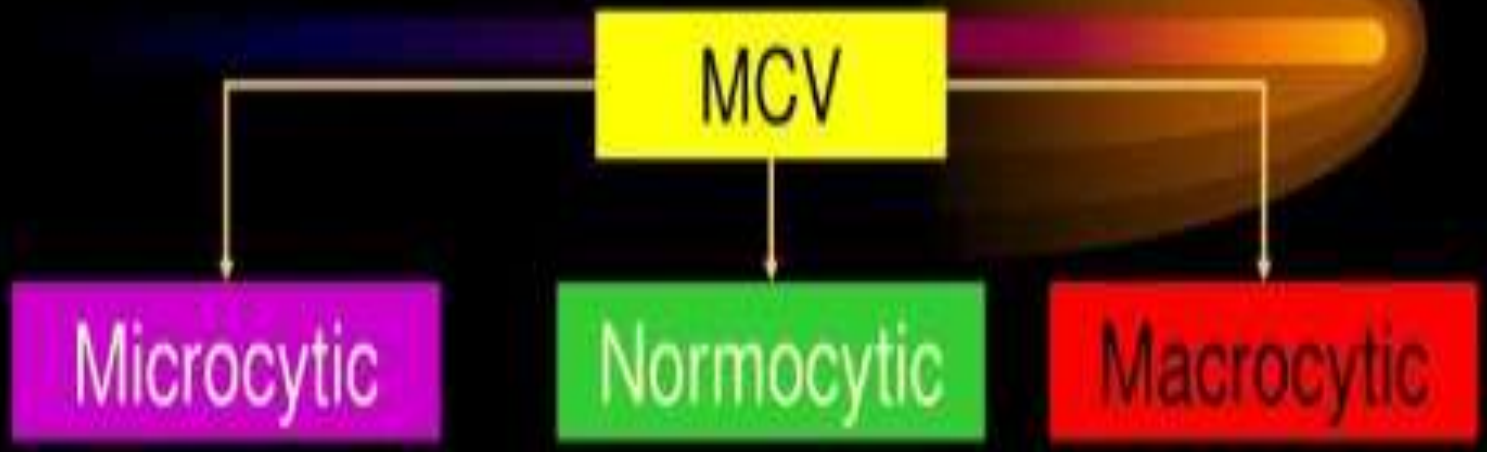
Impaired Red Cell Production

Disturbed proliferation and differentiation of stem cells: aplastic anemia, pure red cell aplasia
Disturbed proliferation and maturation of erythroblasts
- Defective DNA synthesis: deficiency or impaired use of vitamin B_{12} and folic acid (megaloblastic anemias)
- Anemia of renal failure (erythropoietin deficiency)
- Anemia of chronic disease (iron sequestration, relative erythropoietin deficiency)
- Anemia of endocrine disorders
- Defective hemoglobin synthesis
  - Deficient heme synthesis: iron deficiency, sideroblastic anemias
  - Deficient globin synthesis: thalassemias

Marrow replacement: primary hematopoietic neoplasms (acute leukemia, myelodysplastic syndromes)
Marrow infiltration (myelophthisic anemia): metastatic neoplasms, granulomatous disease

*Morphologic:

- Microcytic (MCV < 80 fl).
- Normocytic (MCV 80-100 fl).
- Macrocytic (MCV > 100 fl).



Microcytic	Normocytic	Macrocytic
Iron Deficiency IDA	Chronic disease	Megaloblastic anemias
Chronic Infections	Early IDA	Liver disease/alcohol
Thalassemias	Hemoglobinopathies	Hemoglobinopathies
Hemoglobinopathies	Primary marrow disorders	Metabolic disorders
Sideroblastic Anemia	Combined deficiencies	Marrow disorders
	Increased destruction	Increased destruction

The approach:

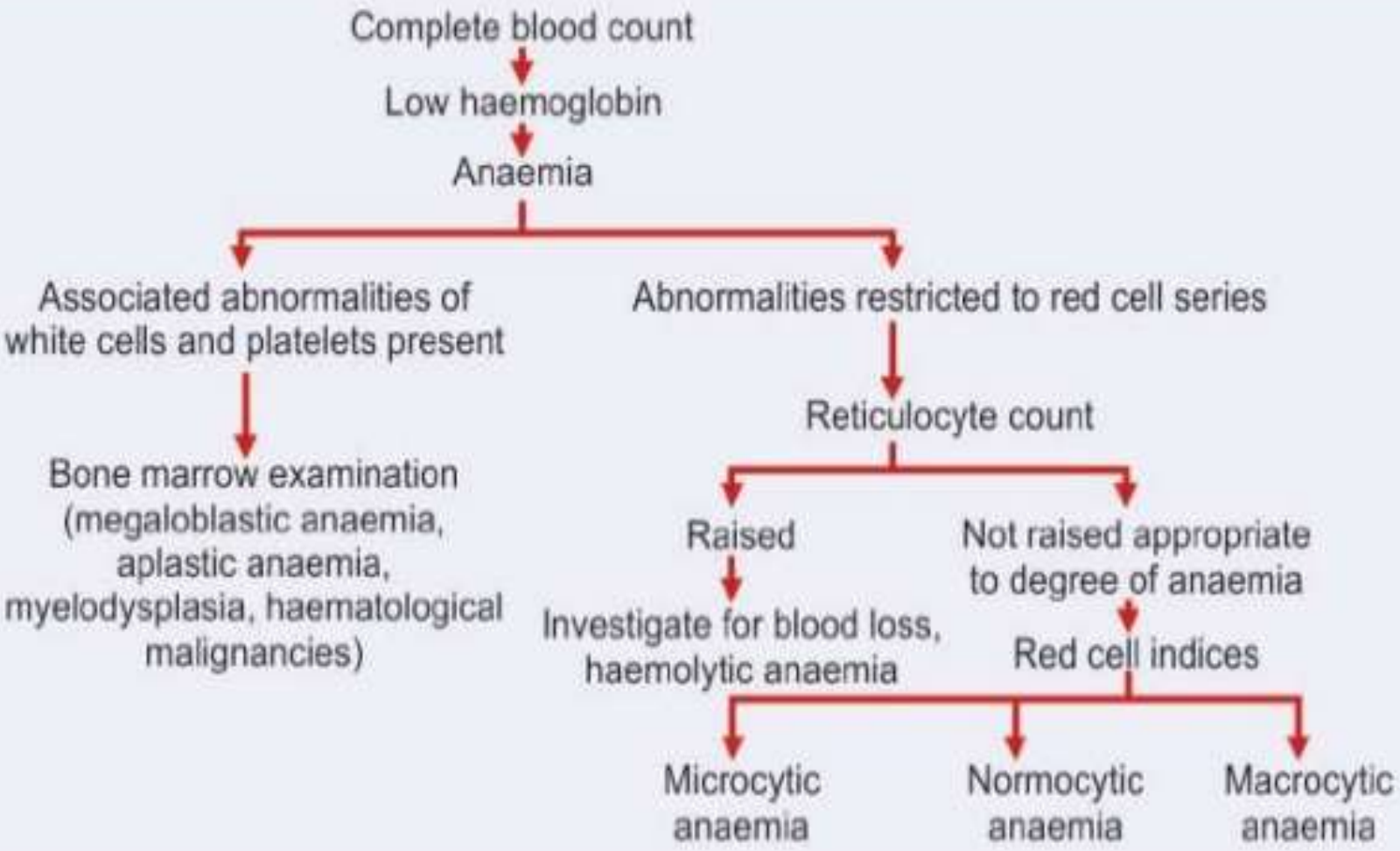
*clinical clues:

- Fainting, pallor…anemia in general
- Jaundice, gallbladder stones, red urine…hemolysis
- Age of presentation, gender, past medical history, family history

The approach:

(1) do CBC/PB smear
(2) Ret. #
(3) MCV, MCH, RDW
(4) BM?

Basic Approach to a diagnosis of anemia



https://www.picswe.com

THE RISK OF Iron Deficiency

IRON DEFICIENCY IS THE MOST COMMON NUTRIENT DEFICIENCY **IN THE WORLD**[1]

4 TO 5 BILLION

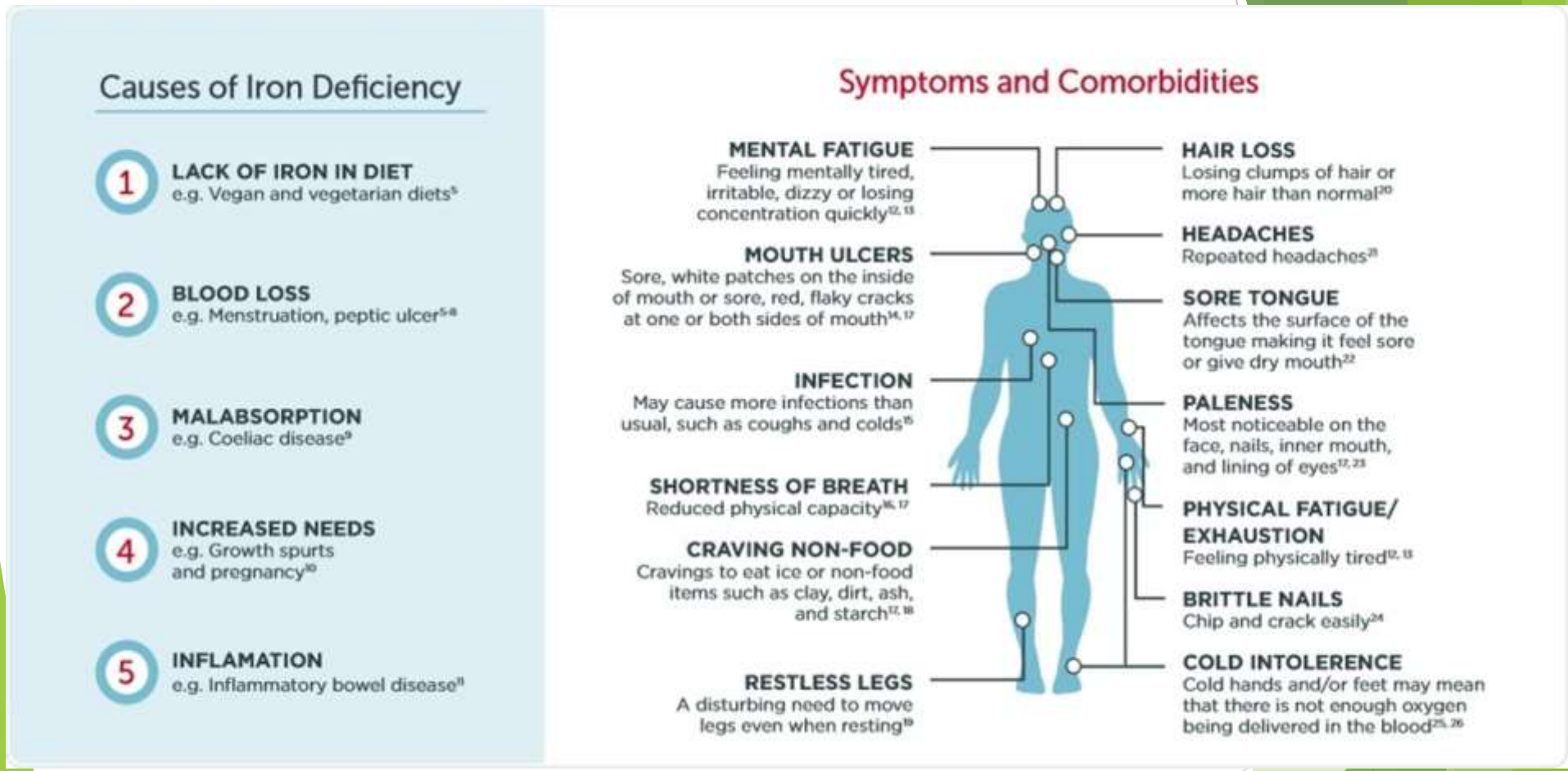
Up to 4 to 5 billion people may suffer from iron deficiency.[2]

Although prevalences can vary across communities, iron deficiency anaemia affects approximately 15% of the world population.[3]

111 MILLION

In the high developed countries, 9.1% of the population is affected resulting in 111 million affected people.[4]

https://www.news-medical.net/news/20161130/Iron-deficiency-an-interview-with-Dr-Thierry-Teil.aspx



https://www.news-medical.net/news/20161130/Iron-deficiency-an-interview-with-Dr-Thierry-Teil.aspx

Iron Deficiency Anemia

- **The normal total body iron mass is about 2.5 g for women and 3.5 g for men.**

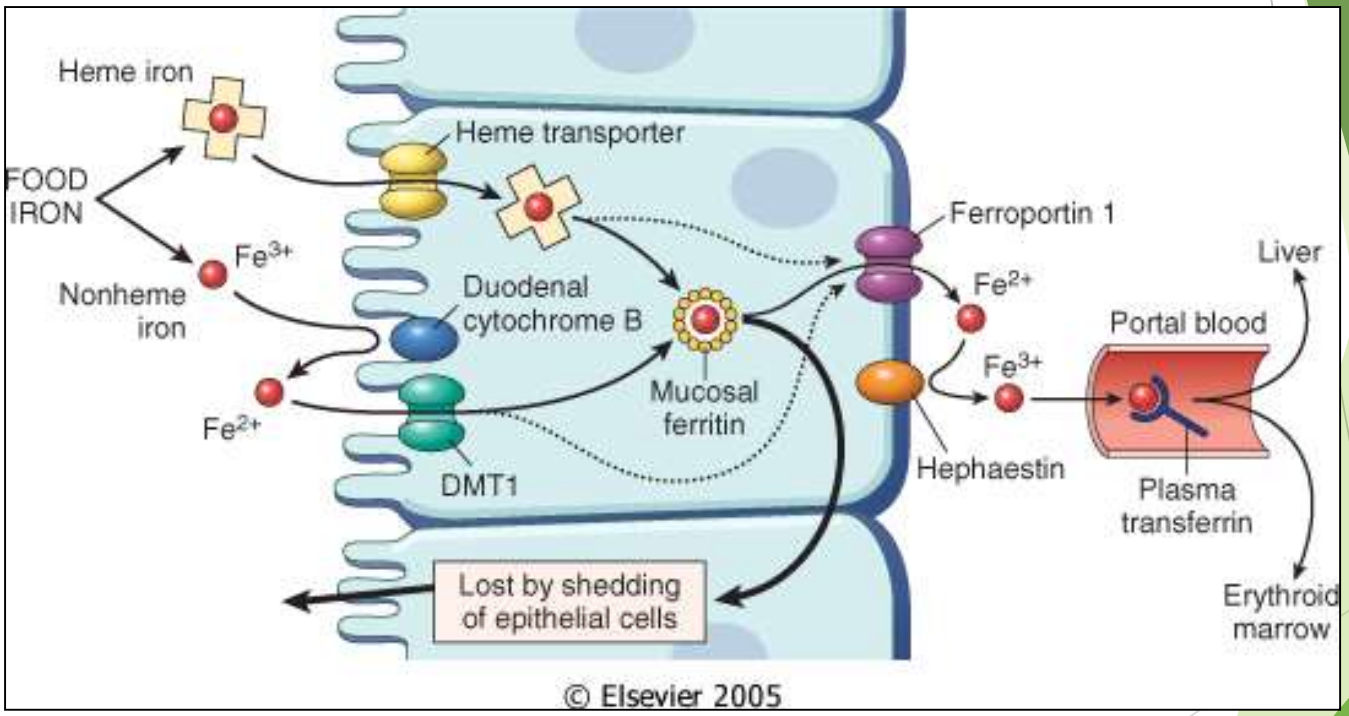
- **Approximately 80% of functional body iron is present in hemoglobin, with the remainder located in myoglobin and iron-containing enzymes (e.g., catalase, cytochromes).**

Iron Deficiency Anemia

- Because serum ferritin is largely derived from this storage pool, the serum ferritin level is a good measure of iron stores.
- Assessment of bone marrow iron is another reliable but more invasive method for estimating iron stores.
- Iron is transported in the plasma bound to the protein transferrin.
- In normal persons, transferrin is about 33% saturated with iron, yielding serum iron levels that average 120 µg/dL in men and 100 µg/dL in women.
- Thus, the normal total iron-binding capacity of serum is 300 to 350 µg/dL.

Ferric +3 to Ferrous+2 (reductase)
DMT1 via apical membrane
Adequate Iron....most iron will handed off to ferritin...shed again
Low iron...basal mambarane via ferroportin
Ferrous+ to Ferric+3 (oxidase)
In plasma via Transferrin

Hepcidin produced by liver..induced by IL-6...Inhibits Ferroportin via internalization and degradation
High Hepcidin...Low Ferroportin...Low iron absorption..more Ferritin



Iron Body Mass:2.5-3.5g
Daily loss: 1-2mg
Absorption:20% of Heme Iron and 1% of non-Heme Iron
Usual diet Iron content: 10-20mg

Iron Deficiency Anemia

- The fraction of iron that is absorbed is regulated by **hepcidin**, a small peptide that is synthesized and secreted from the liver in an iron-dependent fashion.

- In general, high iron levels in the plasma enhance hepcidin production, whereas low iron levels suppress it
- Iron balance maintained by regulating iron absorption/retention

- Hepcidin induced by IL-6

Iron Deficiency Anemia

- Early: decrease in stores (liver, spleen, & BM)

(Ferritin less than 12-300 ng/ml)

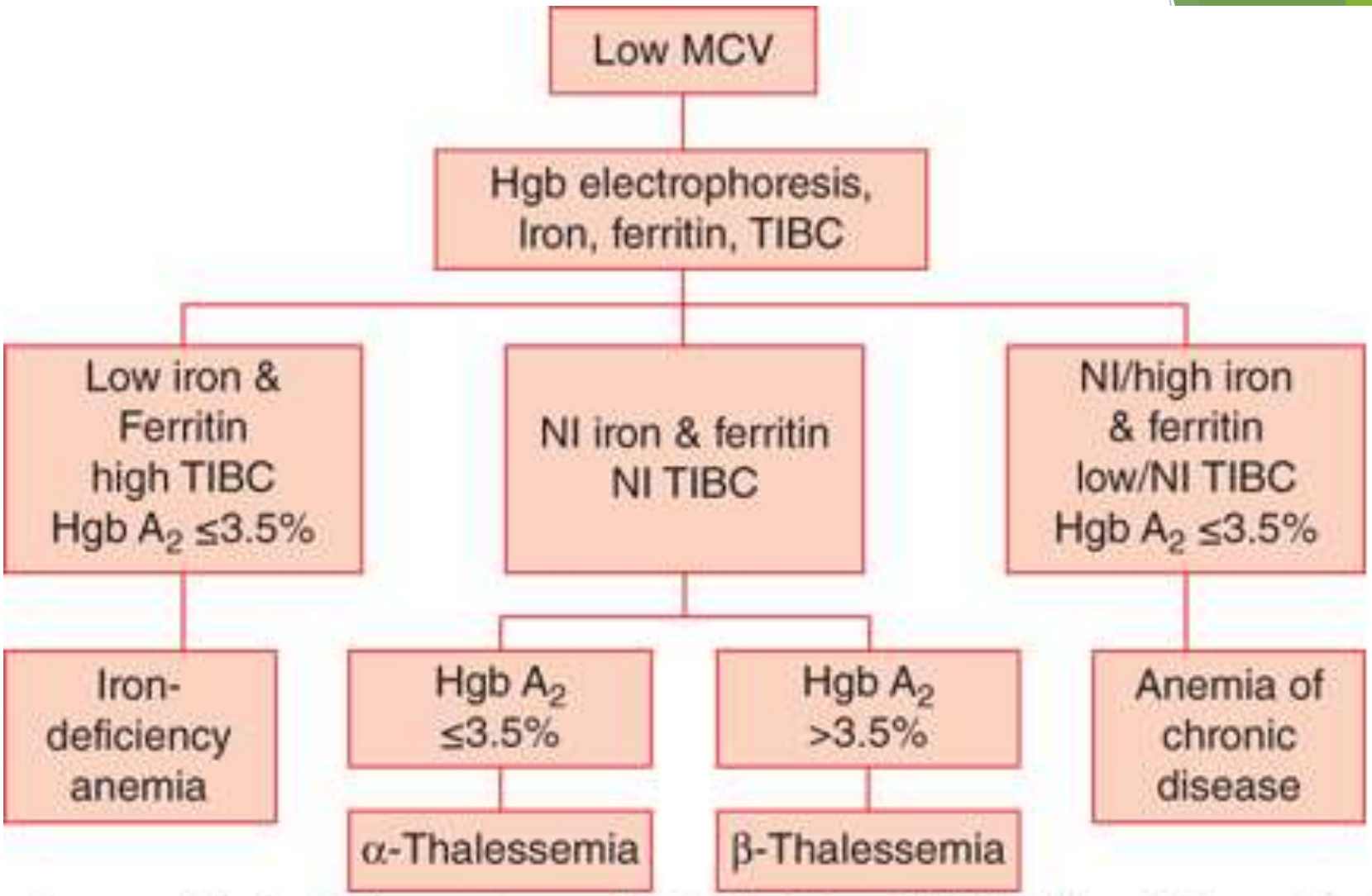
- Decrease in S. Iron
- Increase in Transferrin
- Increase in TIBC
- PB smear changes
- Response to treatment
- BM: normal or slight increase in cellularity

**Transferrin saturation (S.Iron/TIBC) less than 15%.*

Anemia of chronic disease: Disordered iron metabolism as manifested by a low serum iron, decreased serum transferrin, decreased transferrin saturation, increased serum ferritin, increased reticuloendothelial iron stores, increased erythrocyte-free protoporphyrin, and reduced iron absorption, is a characteristic feature of the anemia of chronic disease and has been thought to be a major factor contributing to the syndrome

Importance of Diagnosis:

- It is easy to treat.
- It may be the earliest manifestation of a serious underlying diseases (10-20% of iron deficient patients have cancer, up to 50% have GER/PUD).
- Save unnecessary tests/treatments.



Source: Luis D. Pacheco, George R. Saade, Gary D.V. Hankins: Maternal Medicine
www.obgyn.mhmedical.com

THE END

GOOD LUCK