BLOOD PHYSIOLOGY

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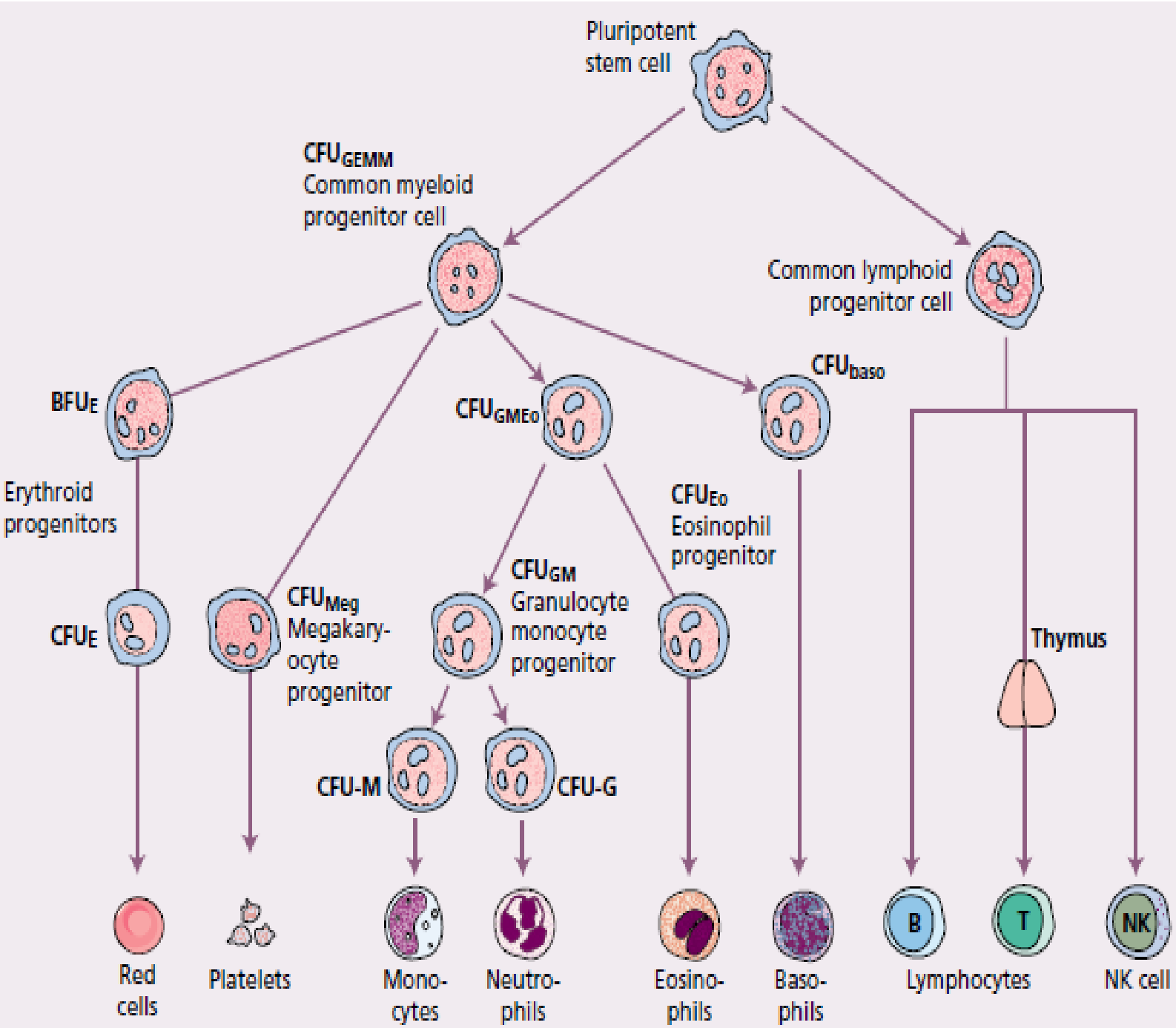
HEMOPOIESIS

- It is a **generation** of blood cells that mainly occur in the bone marrow confined in adult to the central skeleton but in infants and young children extends down the long bones of the arms and legs.
- **Stem cells** divide and differentiate into the different cell types (red blood cell ,white blood cells & platelets) under control of growth factors.
- Main **function** of blood cells:

Table 1.1: Main functions of formed elements of blood

Type of blood cell	*Main function*
Red blood cells	Delivery of oxygen to tissues
White blood cells	Defence against infectious organisms
Lymphocytes	Immune regulation
Platelets	Hemostasis

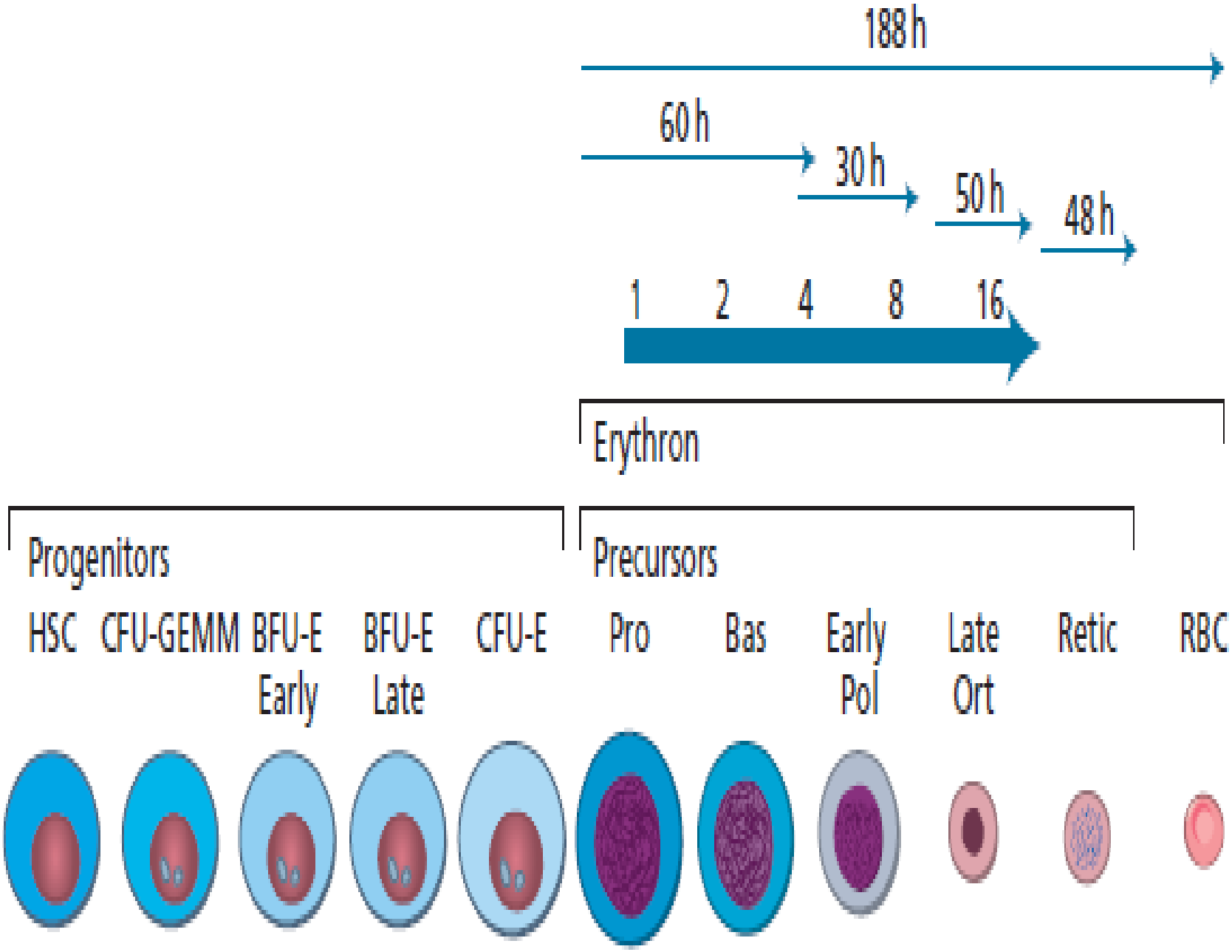
- hematopoiesis **require** frequent building material such as amino acids, carbohydrates, lipids, vitamin B12, folate, vitamin C, and iron.
- Generally, **blood cells** are relatively short-lived cells with a life span ranging from few hrs. to several wks. causing the need for a sustained replacement of functional erythroid, lymphoid and myeloid cells.
- Blood represent the **life sustaining substance** without circulation of blood in the body, organs and tissues quickly stop to function and die.
- The blood **transports life sustaining** elements such as oxygen, glucose, proteins, vitamins, enzymes, and electrolytes to every living cell in the body through arteries, veins, and capillaries
- Blood is 54% **water based plasma**, 1% **white blood** cells and platelets, and 45% **red cells**.


Pluripotent stem cell
CFU$_{GEMM}$ Common myeloid progenitor cell
Common lymphoid progenitor cell
BFU$_E$
CFU$_{GMEo}$
CFU$_{baso}$
Erythroid progenitors
CFU$_{Eo}$ Eosinophil progenitor
CFU$_E$
CFU$_{Meg}$ Megakary-ocyte progenitor
CFU$_{GM}$ Granulocyte monocyte progenitor
Thymus
CFU-M
CFU-G
Red cells
Platelets
Mono-cytes
Neutro-phils
Eosino-phils
Baso-phils
B
T
NK
Lymphocytes
NK cell

RED BLOOD CELLS

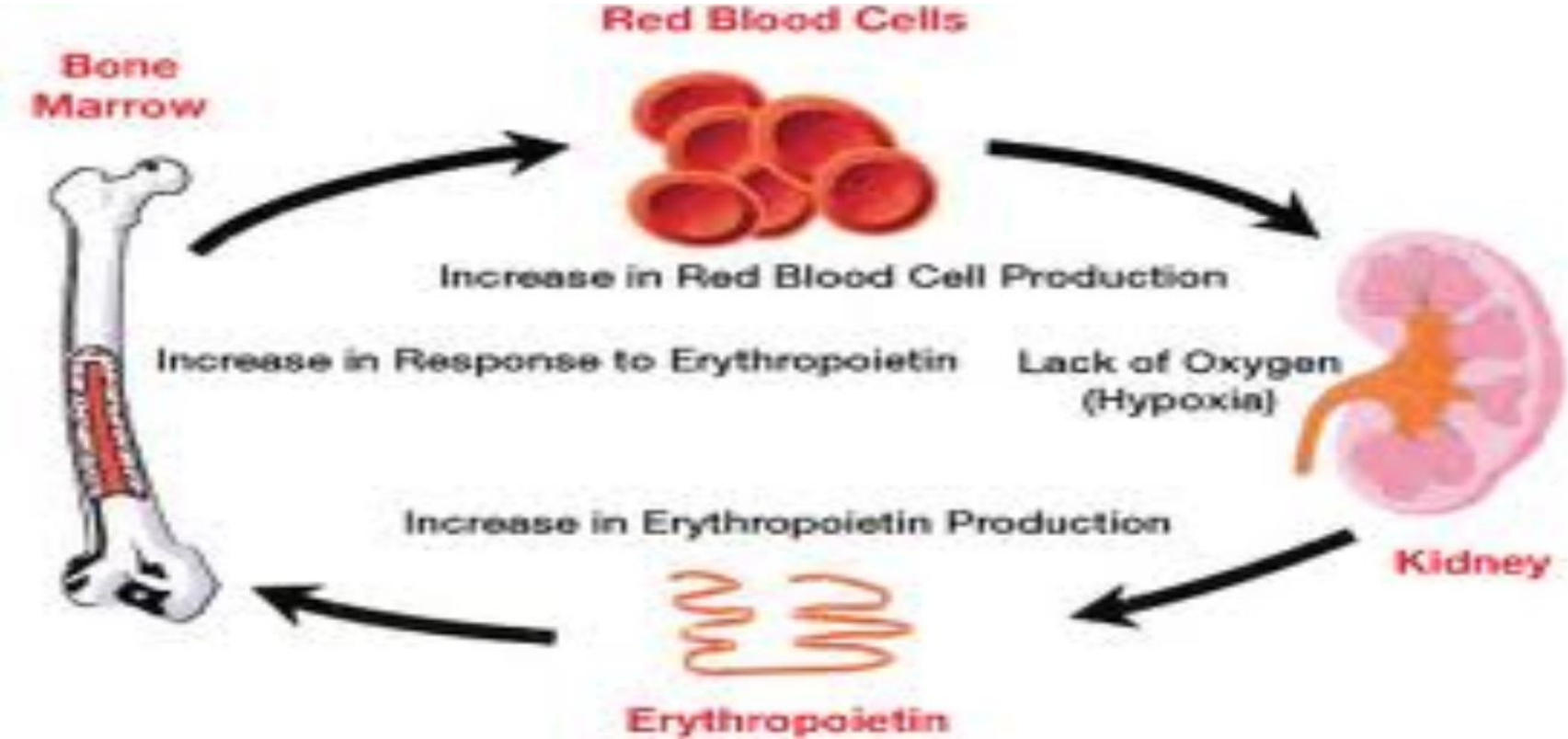
- Are the **predominant cellular** component of blood and a primarily responsible carrier of oxygen from the lungs to the peripheral tissues and organs returning to the lungs with carbon dioxide as a waste product to be exhaled.
- The red cell **contains** the oxygen carrying protein (**hemoglobin)and enzymes** for energy production.
- It is **biconcave disc shape** (7 - 8 micron size) to able to pass through the small capillary beds (3 - 4 micron size) of the micro vasculature.

- As the red cell matures and forms the hemoglobin necessary for it's life span, the nucleus is extruded and a **reticulocyte is expelled** into the blood circulation.
- This juvenile red cell **(reticulocyte) remain in** blood for 2 days that can be identified by staining with methyline blue. Normal count is between 0.8 and 2.4% of the red cell number. Increase or decrease reflects red cell production by the bone marrow factory.
- If **intense marrow stimulation** occurs, larger stress reticulocytes or shift cells may be observed on the peripheral smear with high count.


188 h
60 h
30 h
50 h
48 h
1
2
4
8
16
Erythron
Progenitors
Precursors
HSC
CFU-GEMM
BFU-E Early
BFU-E Late
CFU-E
Pro
Bas
Early Pol
Late Ort
Retic
RBC

- The normal red cell has a **life span** of 120 days metabolized in the reticuloendothelial system RES(spleen , liver, and bone marrow) and the iron, amino acids, carbohydrate and lipids are recycled.
- **Lysis of red cell** also produce **free Hb** this bind to Haptoglobin for transport to the RES
- A breakdown product of hemoglobin is **bilirubin** which is conjugated in the liver and excreted in the biliary system into the gut. Isolated increase in indirect bilirubin(unconjecated) is a very specific indicator of increased red cell breakdown.

- The **kidney cells secrete** erythropoietin in response to low tissue oxygen levels. Erythropoietin stimulates bone marrow red cell production.
- This **hormonal feedback loop is less responsive** to anemia **in renal disease** and may produce high hemoglobin levels with **chronic hypoxia**



HEMOGLOBIN (HB)

- It is the **predominant protein** in the red cell responsible for transporting oxygen molecules.
- **Three types of Hb** : **(in adult)**

  Hb **A** (97%), **F** or fetal Hb (1%), and Hb **A2** (2%).
- **Fetal hemoglobin**, predominant in utero, strongly binds oxygen facilitating transport from mother to fetus across the placenta.
- **Hb F** usually switch to adult Hb (Hb A) occurs after birth by decrease F and produce A.

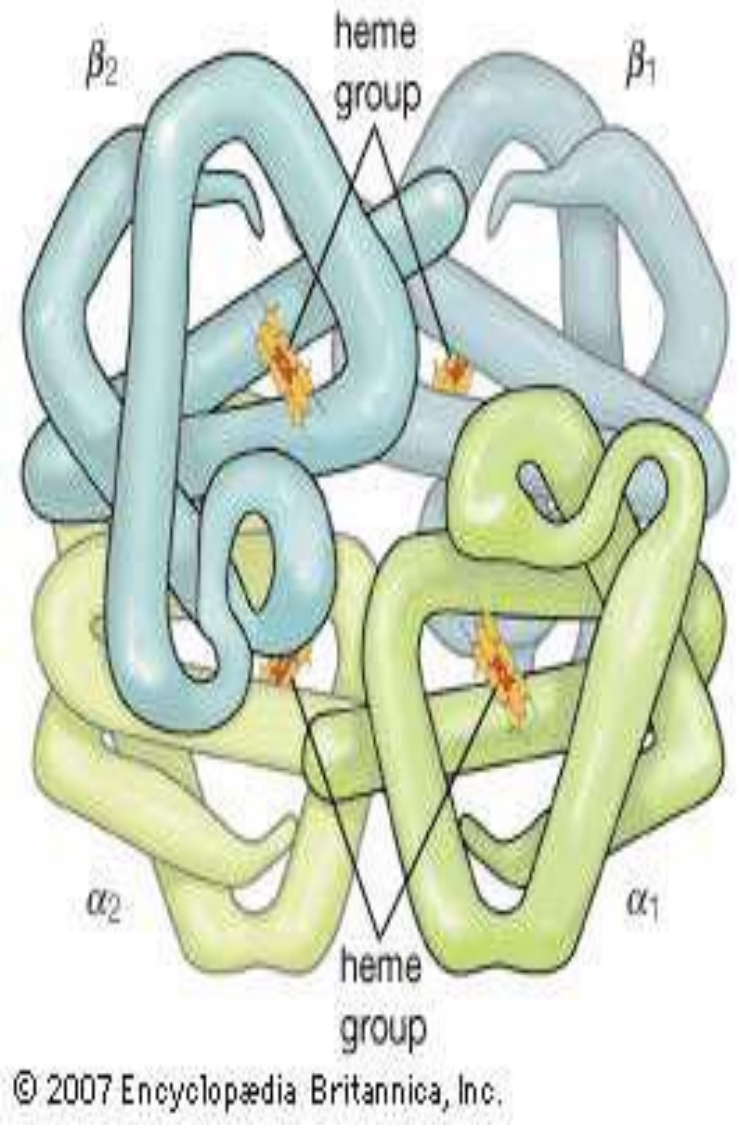
- **Hb A** predominant Hb after one year of birth is composed of **2 beta** globin chains and **2 alpha** globin chains bonded to four iron containing heme groups.
- **Hb production** requires **iron** , the synthesis of the protoporphyrin ring and production of the globin chains so reductions in any of these leading to develop anemias.
- **The globin chains** are protein made up of a precise sequence of amino acids that are coded by genes located on chromosome16 and chromosome 11 contained in the nucleus of the bone marrow stem cells.

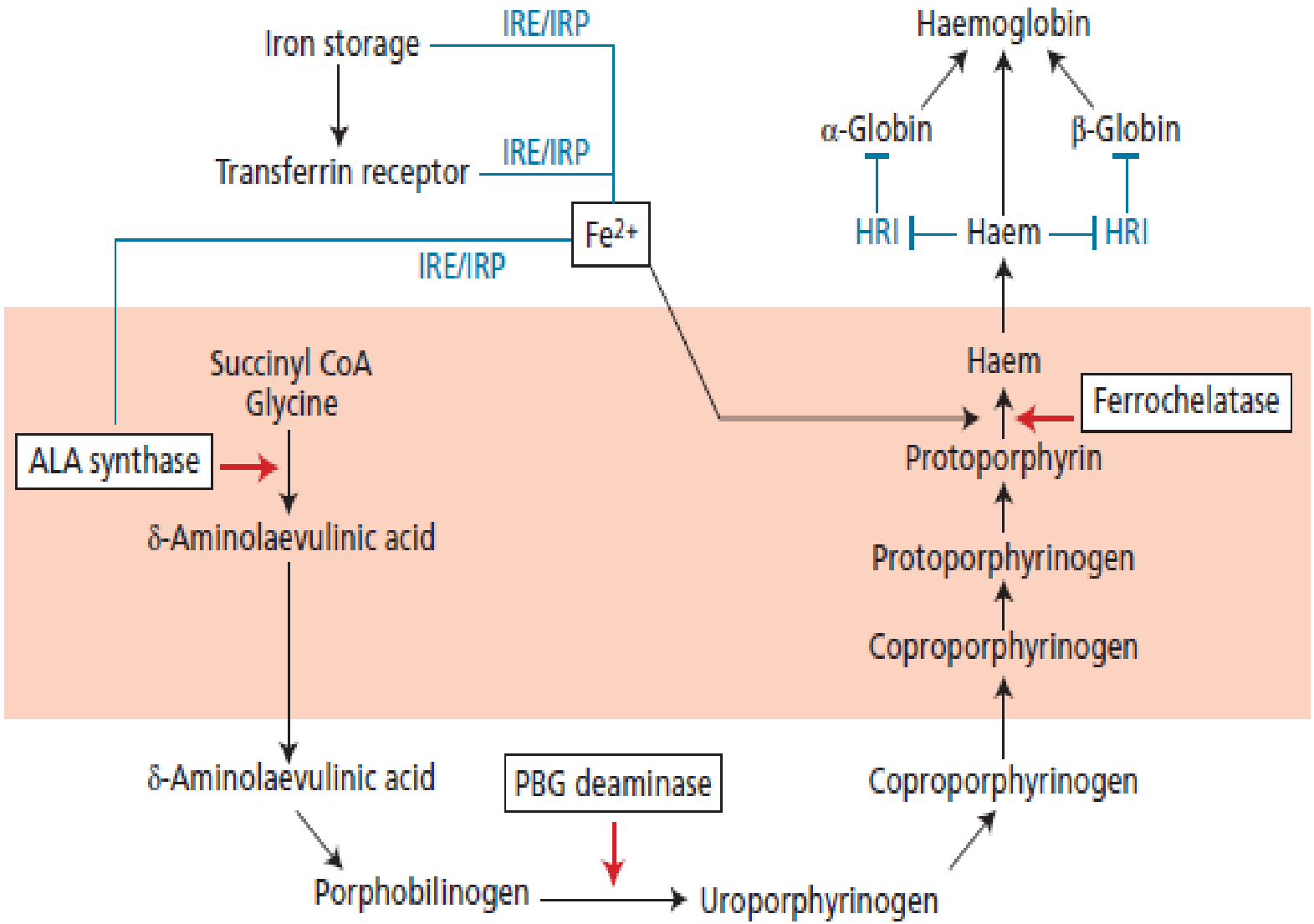
Types of human Hb

Haemoglobin proteins

Embryonic	Fetal	Adult
Hb Gower 1	HbF	HbA
ζ ζ ε ε	α α Gγ Gγ	α α β β
Hb Gower 2		HbA2
α α ε ε	α α Aγ Aγ	α α δ δ
Hb Portland		
ζ ζ γ γ		

Hb structure




Iron storage
IRE/IRP
Transferrin receptor
IRE/IRP
Fe2+
IRE/IRP
Haemoglobin
α-Globin
β-Globin
HRI
Haem
HRI
Succinyl CoA
Glycine
ALA synthase
δ-Aminolaevulinic acid
Haem
Ferrochelatase
Protoporphyrin
Protoporphyrinogen
Coproporphyrinogen
δ-Aminolaevulinic acid
PBG deaminase
Coproporphyrinogen
Porphobilinogen
Uroporphyrinogen

ANEMIA

- Anemia is from the **Greek** word anaimia, meaning without blood.
- Anemia is **defined** as a reduction in the number of red blood cells, blood hemoglobin content, or hematocrit.
- There are **three primary causes** of anemia:
  1. **reduced production** of red blood cells in the bone marrow factory such as IDA
  2. **excessive destruction** of red blood cells such as hemolytic anemia
  3. **excessive blood loss** as in bleeding

WHO Grading of anemia

- Grade 1 (Mild Anemia): 10 g/dl
- Grade 2 (Moderate Anemia): 7-10 g/dl
- Grade 3 (Severe Anemia): below 7 g/dl

DIAGNOSIS OF ANEMIA

- The **diagnostic approach** should contain :

1) History:

- History of melena, abdominal pain, Aspirin or non-steroidal anti-inflammatory agents (NSAIDs) use, anticoagulant use, past peptic ulcer disease, then consider GI bleeding or platelet dyfunction.
- History of poor diet ,pica then consider iron or folate deficiency, and general malnutrition
- History of gastric surgery, distal paresthesias, gait problems -consider B12 deficiency
- Family history of blood cell disorder: consider Sickle Cell disease, G6PD,and Thalassemia

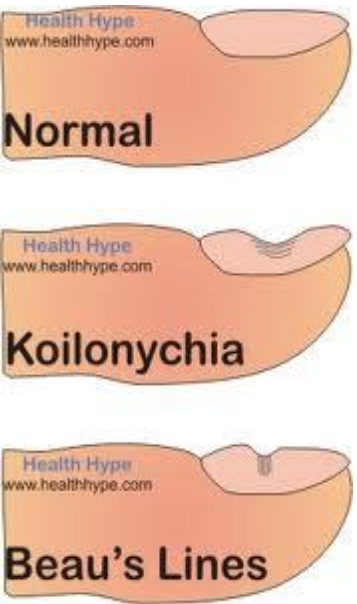
2) Physical examination

- Anemia is clinically suspected by the presenting symptoms and signs of weakness, fatigue, palpitations, increased heart rate, dyspnea, positional dizziness, syncope, bleeding from any site, increased or new onset angina.
- It may be suspected when the physical findings of tachycardia ,orthostasis , pallor, or jaundice are observed.
- Specific signs are associated with particular types of anemia, e.g. koilonychia (spoon nails) with iron deficiency, jaundice with haemolytic or megaloblastic anaemias , decreased vibratory and position sense seen in B12 deficiency.

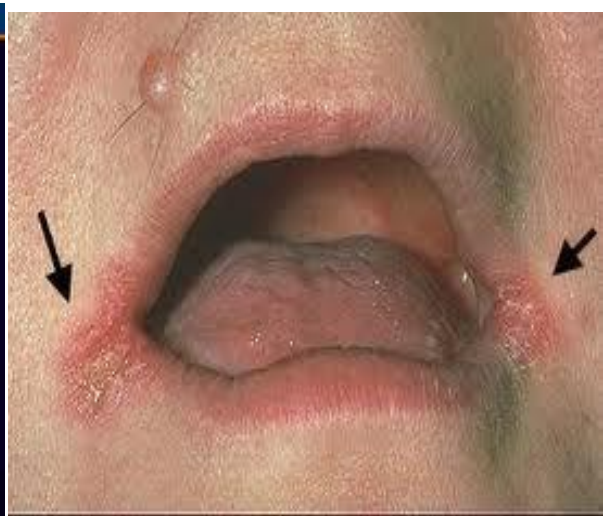
(a)

(b)

Pallor of the conjunctival mucosa (a) and of the nail bed (b) in two patients with severe anaemia (haemoglobin 6.0 g/dL).



Koilonychia



Angular cheilitis

3) laboratory evaluation

1. Complete blood count

PARAMETER	NORMAL ADULT	COMMENTS
HB - Hemoglobin	Male= 15.5 +/- 2mg/dl Female = 13.5 +/- 2	Low = Anemia High = Polycythemia
HCT - Hematocrit	Male= 46.0 +/- 6% Female= 41.0 +/- 6%	= =
RBC-Red Blood cell count	Male = 4.3-5.9 Million/uL Cell Count Female= 4.0 - 5.2	= =
WBC - White Blood Cell Count	4.5-11K/uL	Low = Leukopenia High = Leukocytosis
Platelet Count	150 - 400 K cell/uL	Low =Thrombocytopenia High = Thrombocytosis
Retic - Reticulocyte Count	0.5 -1.5 % 25 - 85 K cell/ul	Low in anemia = low High = RBC loss

2. Red cell indices

- **MCV** :Mean corpuscular volume of RBC

  Low = Microcytosis , **High** = Macrocytosis.
- **MCH** :Mean corpuscular hemoglobin of RBC

  Low = Hypochromic , **High** = Hyperchromic
- **MCHC** :Mean corpuscular hemoglobin concentration

  Low = R/O Fe Deficiency, **High** = R/O Sperocytosis
- **RDW** :Red cell distribution width

  Variation in RBC size

	At birth	*Men*	*Women*
Red cell indices			
MCV	100-120 fL	82-100 fL	82-100 fL
MCH	31-37 pg	27-32 pg	27-32 pg
MCHC	30-36 gm/dL	31-35 gm/dL	31-35 gm/dL
RDW	13-18%	11.5-14.0%	11.5-14.0%

3. **Blood film** : for red cell morphology

	Red cell abnormality	Causes
	Normal	
	Macrocyte	Liver disease, alcoholism. Oval in megaloblastic anaemia
	Target cell	Iron deficiency, liver disease, haemoglobinopathies, post-splenectomy
	Stomatocyte	Liver disease, alcoholism
	Pencil cell	Iron deficiency
	Echinocyte	Liver disease, post-splenectomy. storage artefact
	Acanthocyte	Liver disease, abetalipo-proteinaemia, renal failure

	Red cell abnormality	Causes
	Microspherocyte	Hereditary spherocytosis, autoimmune haemolytic anaemia, septicaemia
	Fragments	DIC, microangiopathy, HUS, TTP, burns, cardiac valves
	Elliptocyte	Hereditary elliptocytosis
	Tear drop poikilocyte	Myelofibrosis, extramedullary haemopoiesis
	Basket cell	Oxidant damage– e.g. G6PD deficiency, unstable haemoglobin
	Sickle cell	Sickle cell anaemia
	Microcyte	Iron deficiency, haemoglobinopathy

4. S .iron ,Transferrin, Ferritin
5. Folate & B12 level
6. Bilirubin
7. Lead level
8. Hemoglobin Electrophoresis
9. Reticulocyte count
10. LFT
11. RFT
12. Bone marrow sprite & biopsy


THANK YOU