HAEMOGLOBIN

DR NILESH KATE

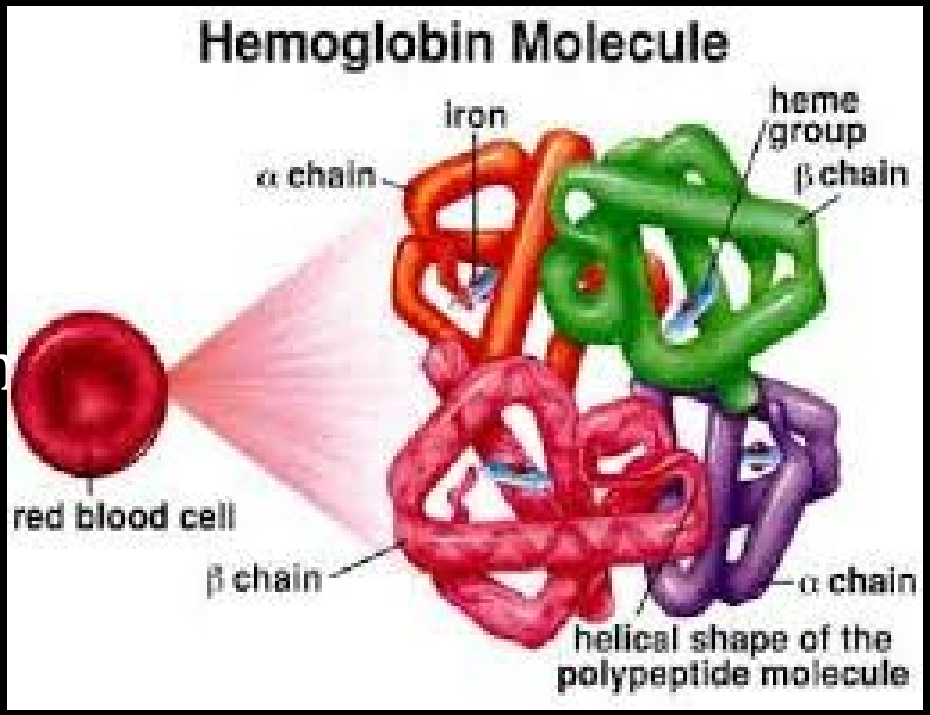
MBBS, MD

ASSOCIATE PROF

DEPT. OF PHYSIOLOGY

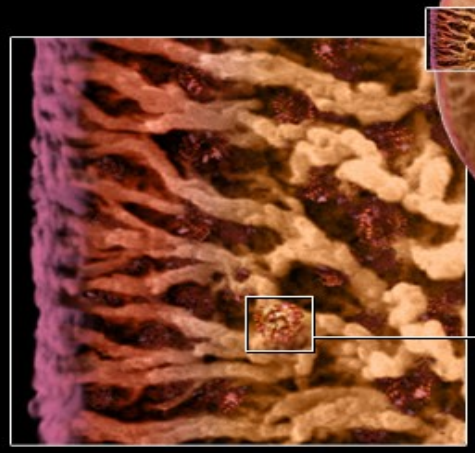
At the End of Class

- Haemoglobin
- Structure, function, variations
- Derivatives, synthesis an degradation of hemoglobin.
- Anemia – Types with example, c/f , treatment

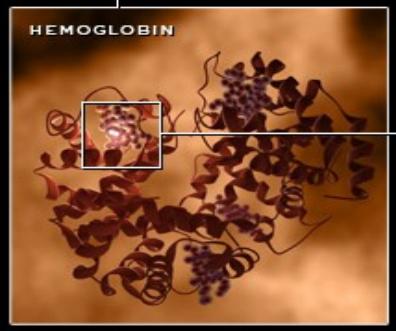


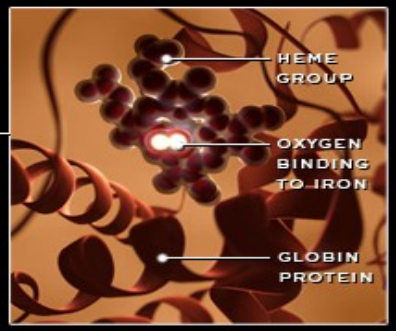
Haemoglobin

$(C_{712}H_{1130}O_{245}N_{214}S_2Fe)_4$



The red blood cell consists of a sponge-like, protein rich frame. This frame houses hemoglobin molecules. The rest of the cell is composed of fatty substances that support hemoglobin production.

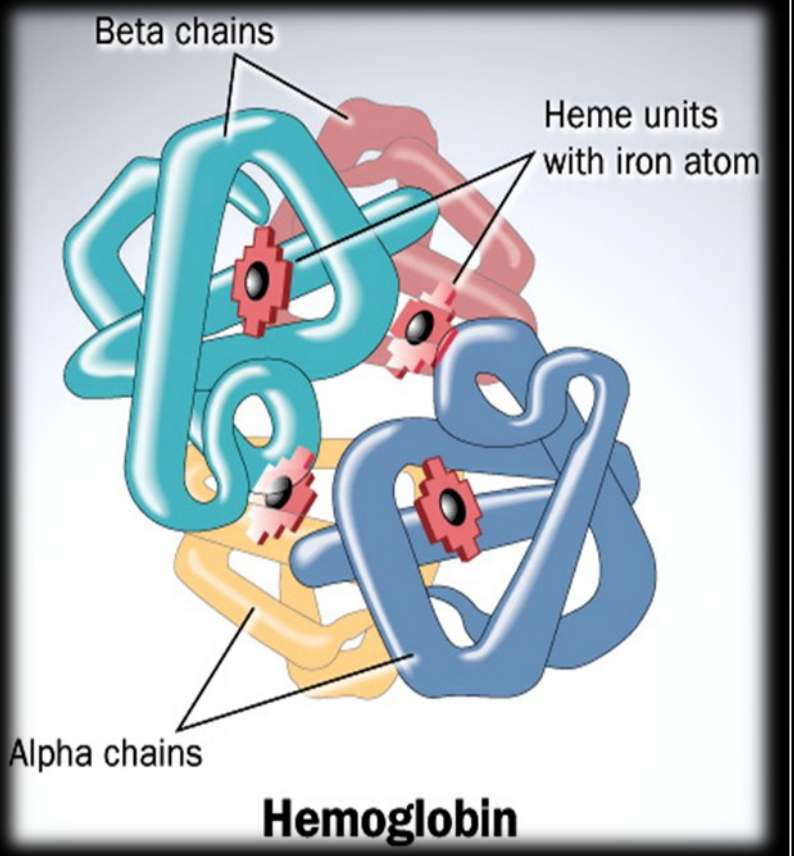




A heme group consists of an iron atom bound equally to four nitrogen atoms, all laying in one plane. This iron atom is the site of oxygen binding.

HAEMOGLOBIN

- It is a **Red** pigment
- Present in RBC of Blood.
- It is a conjugated protein, & **Chromoprotein**.
- It is made up of Iron and Protein
- It's molecular weight is 68000.



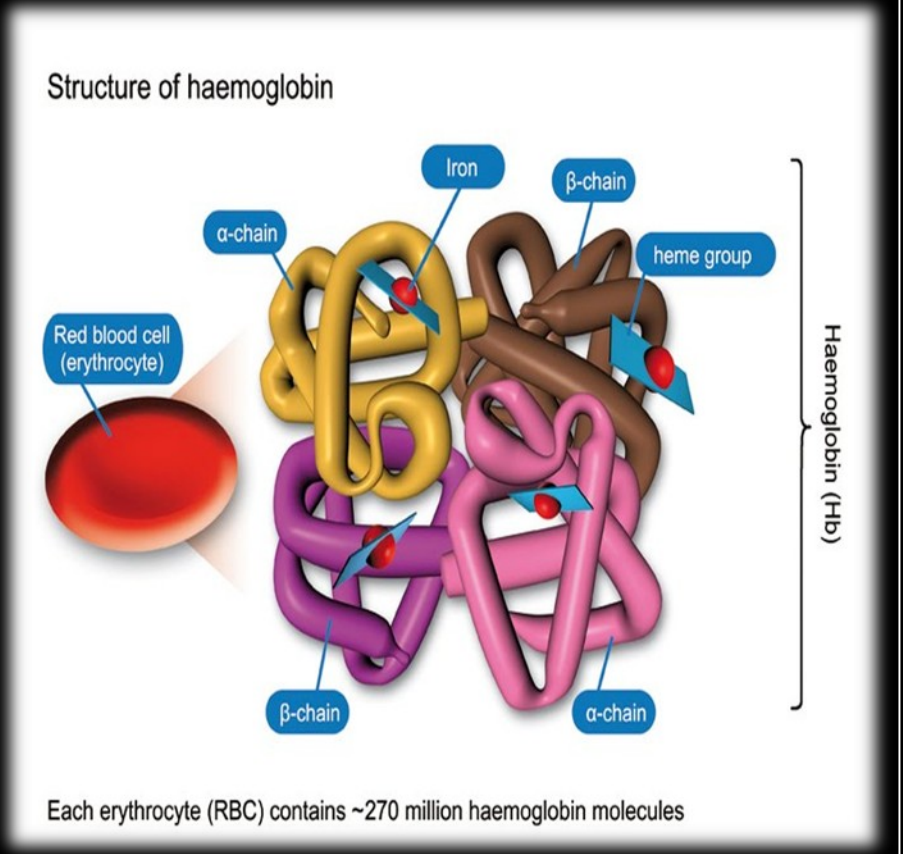
Disadvantages if haemoglobin present in plasma.

- Increase viscosity.
- Increase osmotic pressure.
- Rapid destruction by reticuloendothelial system.
- Haemoglobinuria

(excretion through kidney)

NORMAL VALUES OF HEMOGLOBIN

- The Normal Hb level:
- **Fetus** – 16-18 gm/dl
- **Newborn** – 20-24 gm/dl.
  - Transfusion from placenta
  - Haemoconcentration

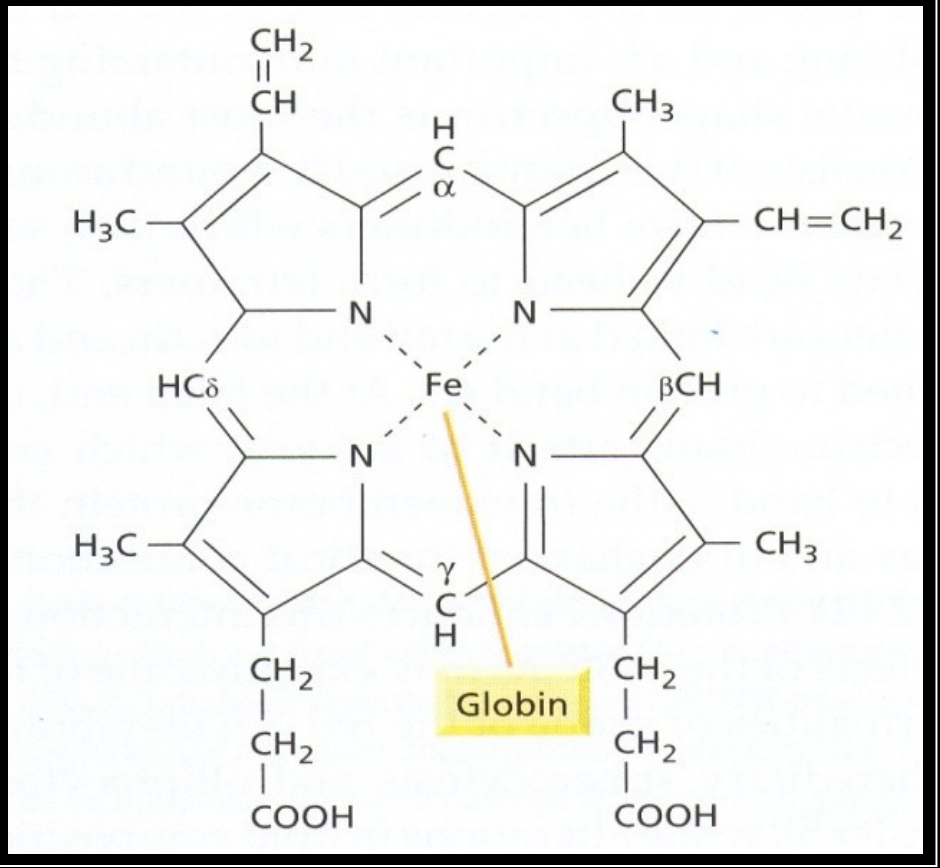


NORMAL VALUES OF HEMOGLOBIN

- **1 year** – 10-12 gm/dl
- **Males** - 14 – 17 gm/100ml
  Females- 12 – 15 gm/100ml

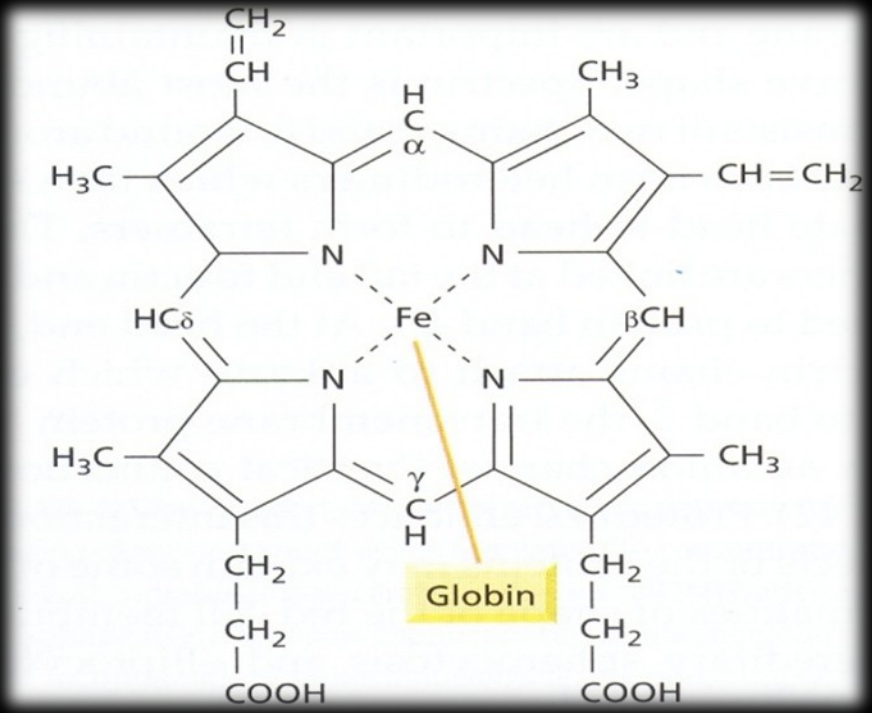
STRUCTURE OF HAEMOGLOBIN.

- Iron containing pigment called **Haem** attached with protein – **Globin**.
- Haeme is Iron – porphyrin complex called **IRON-PROTOPORPHYRIN IX.**
- **Globin – Protein.**



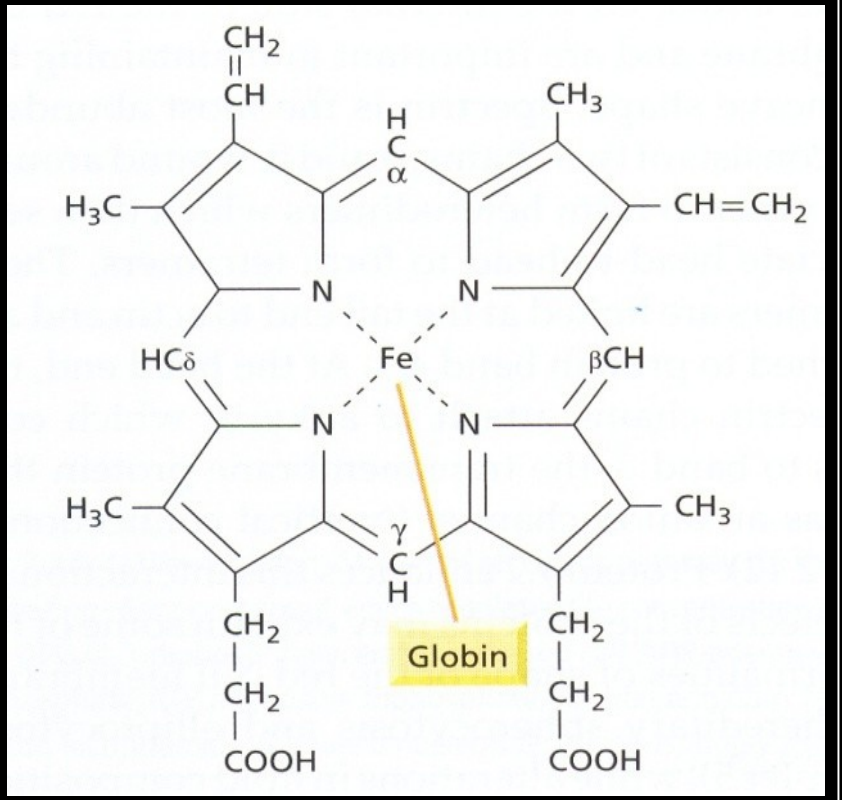
STRUCTURE OF HAEME IRON-PROTOPORPHYRIN IX.

- **IRON**
  - Ferrous form (Fe2+).
  - Iron attached to nitrogen atom of each pyrrole ring.
  - On iron loose bond for
    - Oxygen
    - Carbon monoxide.



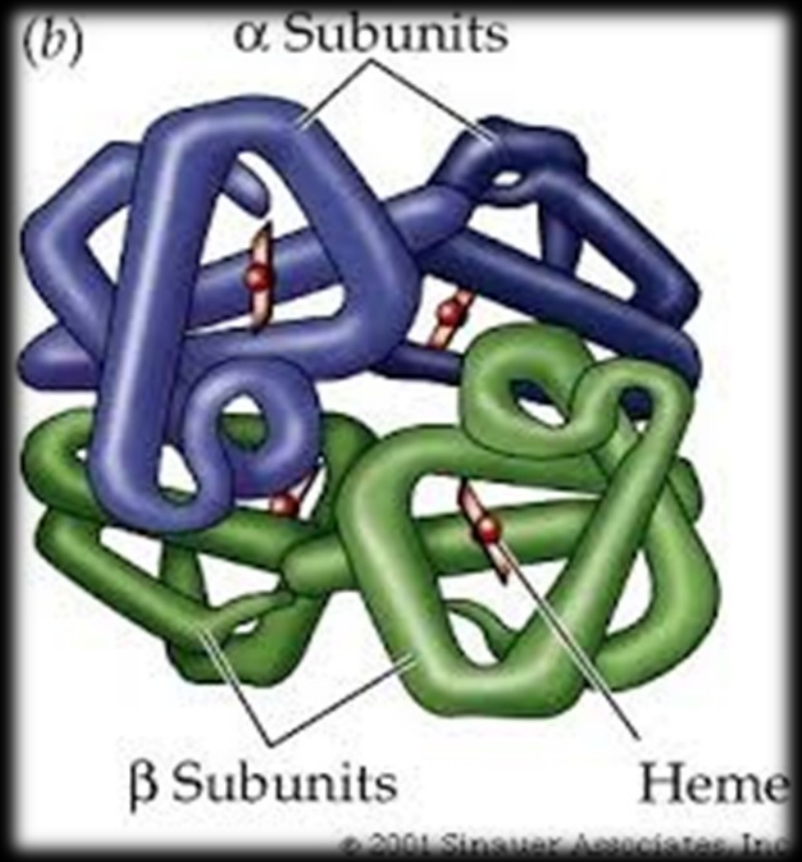
STRUCTURE OF HAEME IRON-PROTOPORPHYRIN IX.

- Porphyrin nucleus.
- **4 Pyrrole Rings (Tetrapyrrole)**
- **Bridges** – Methine (CH)
- **Side chains** – 8
  - Methyl (CH3) - 4
  - Vinyl (CH.CH2) - 2
  - Propionic acid - 2 (CH2.CH2.COOH)



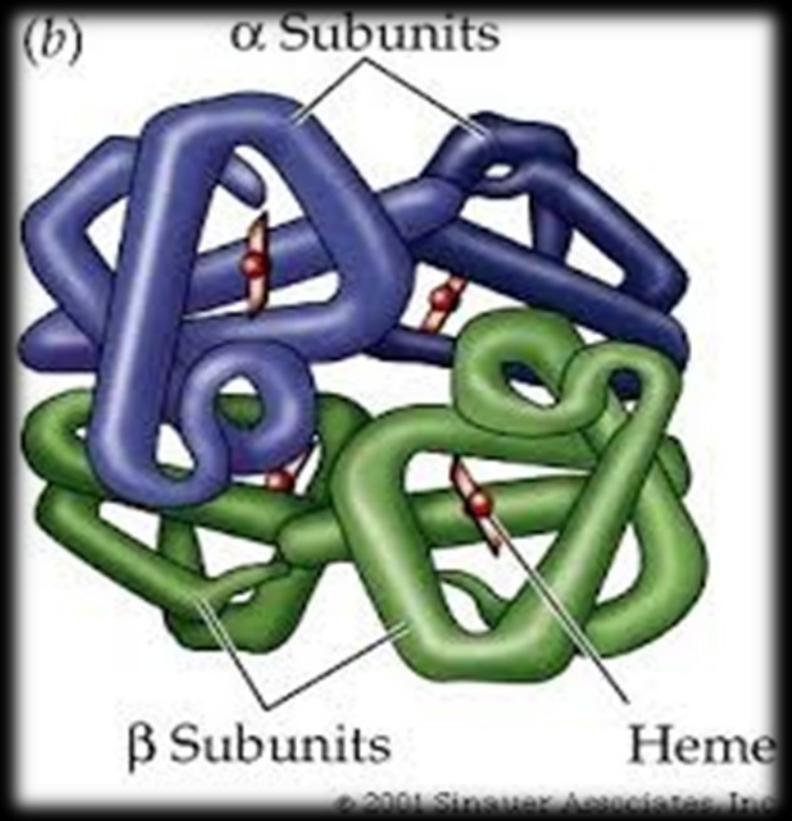
Structure of Globin.

- Made up of 4 polypeptide chains.
- Globin is HbA
- 2 **alpha** chains ( ) – 141 amino acids
- 2 **Beta** chains ( ) – 146 amino acids.



Attachment of Haeme to Globin.

- 4 units of Haeme attached to 1 unit of Globin.
- So 1 **Haemoglobin** molecules contains **4 Iron Atoms** which carry **4 molecules of oxygen**.



Synthesis of Hemoglobin

i) 2 succinyl – CoA + 2 glysine → Pyrrole

ii) 4 Pyrrole → Protoporphyrin IX

iii) Protoporphyrin IX + Fe2+ → Heme

iv) Heme + Polypeptide → Hemoglobin chain (α or β)

v) 2 α chains + 2 β chains → Haemoglobin A.

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- Succinyl-CoA Glycine

Pyridoxal phosphate

- αAmino -β-ketoadipic acid

ALA synthetase

- α amino-δ-Laevulinic acid
  - *ALA dehydrogenase.*
- Porphobilinogen
- Protoporphyrin IX

ferrous

- Haem

globin

- haemoglobin

Factors controlling Haemoglobin formation.

- **Role Of Proteins** – First class proteins provide amino acids.
- **Most imp** – food of animal origin, liver, spleen, kidney & heart
- **Intermediate value** – muscles
- **Least** – cereals, dairy products, veg & fruits.

ROLE OF IRON.

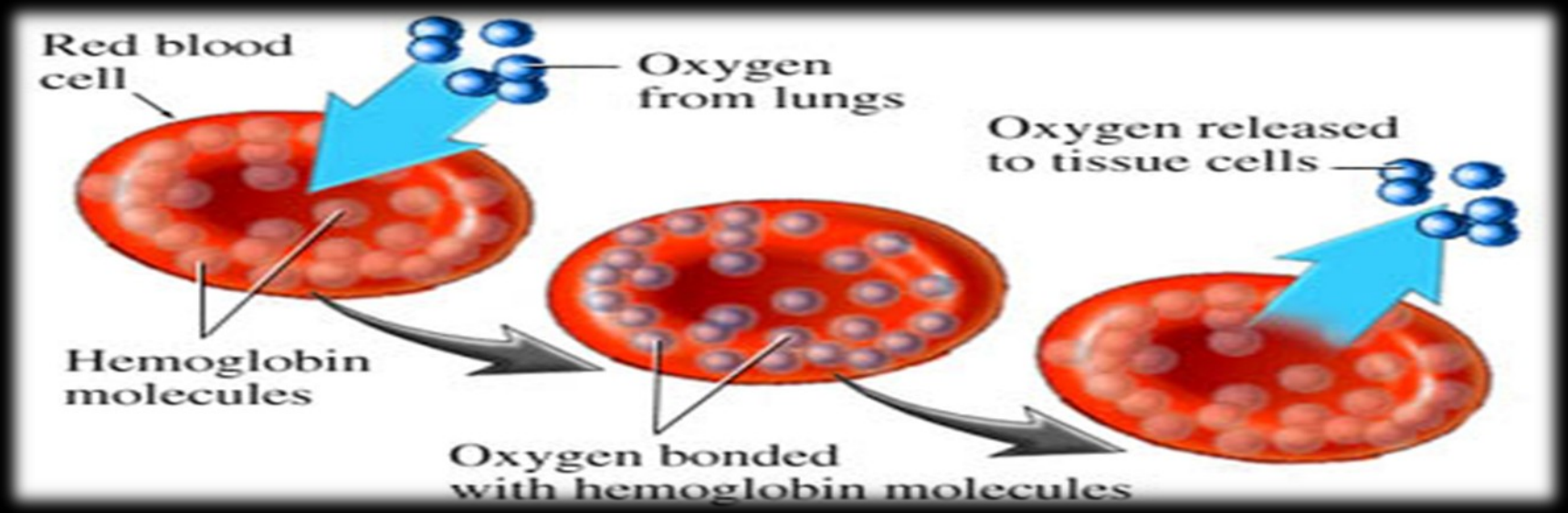
- Important for formation of Haeme part of Haemoglobin.
- **Sources of iron** – Dietary iron
- **Other sources** – Iron released from degradation of RBC.

Role of other metals

- **Copper** – Promotes Absorption, Mobilization & Utilization of iron.
- **Cobalt** – Increases production of **Erythropoietin**.
- **Calcium** – conserve iron & subsequent utilization.
- **Role of vitamins.**
  - Vit B12, Folic acid help in synthesis of nucleic acid.
  - & vit C helps in absorption of iron from gut. (Fe3+ to Fe2+)
- **Role of bile salts.**
  - Imp for proper absorption of copper & nickel.

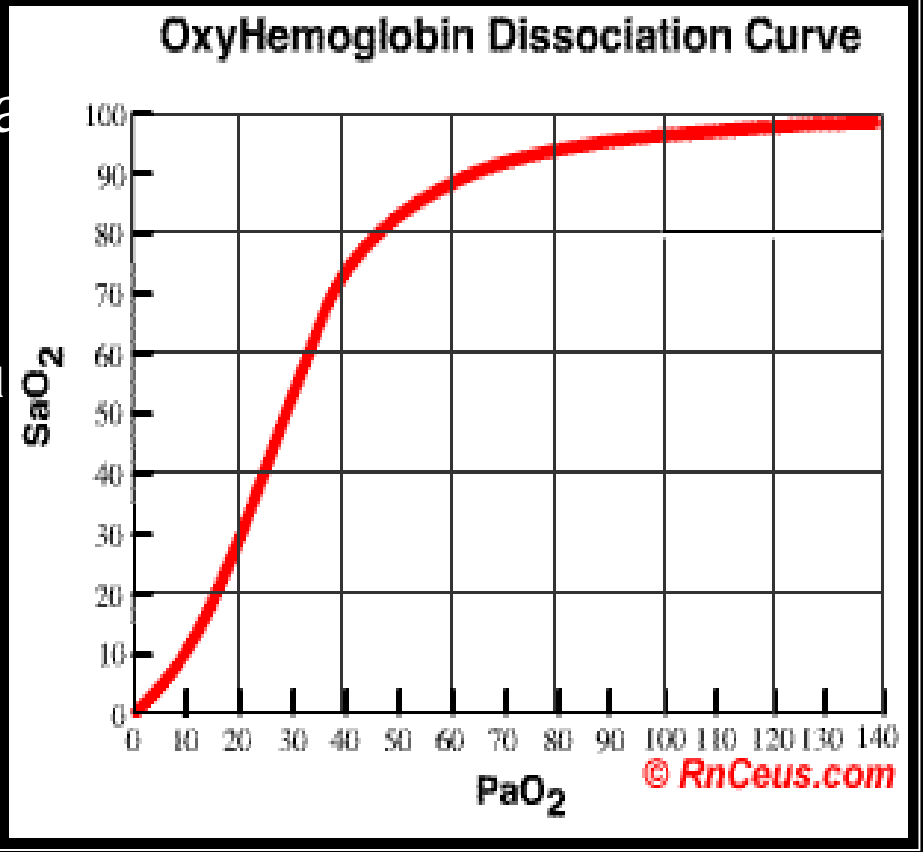
Functions of Haemoglobin

- Transport oxygen to tissues
- Transport Co2 to lungs
- Maintains acid base balance (As a Buffer)

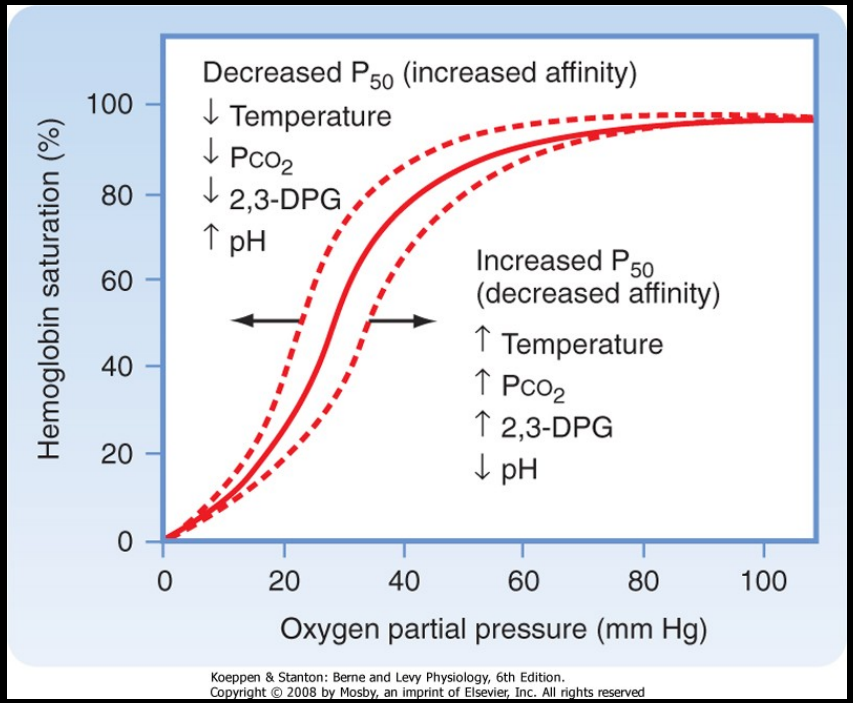


Haemoglobin – Oxygen Binding.

- O2 is attached with haemoglobin reversibly a **6th covalent bond.**
- Oxygenation of 1st haem **increases affinity** for 2nd in turn 3rd & 4th.
- Reason for O2-Hb dissociation curve **Sigmoid shape.**



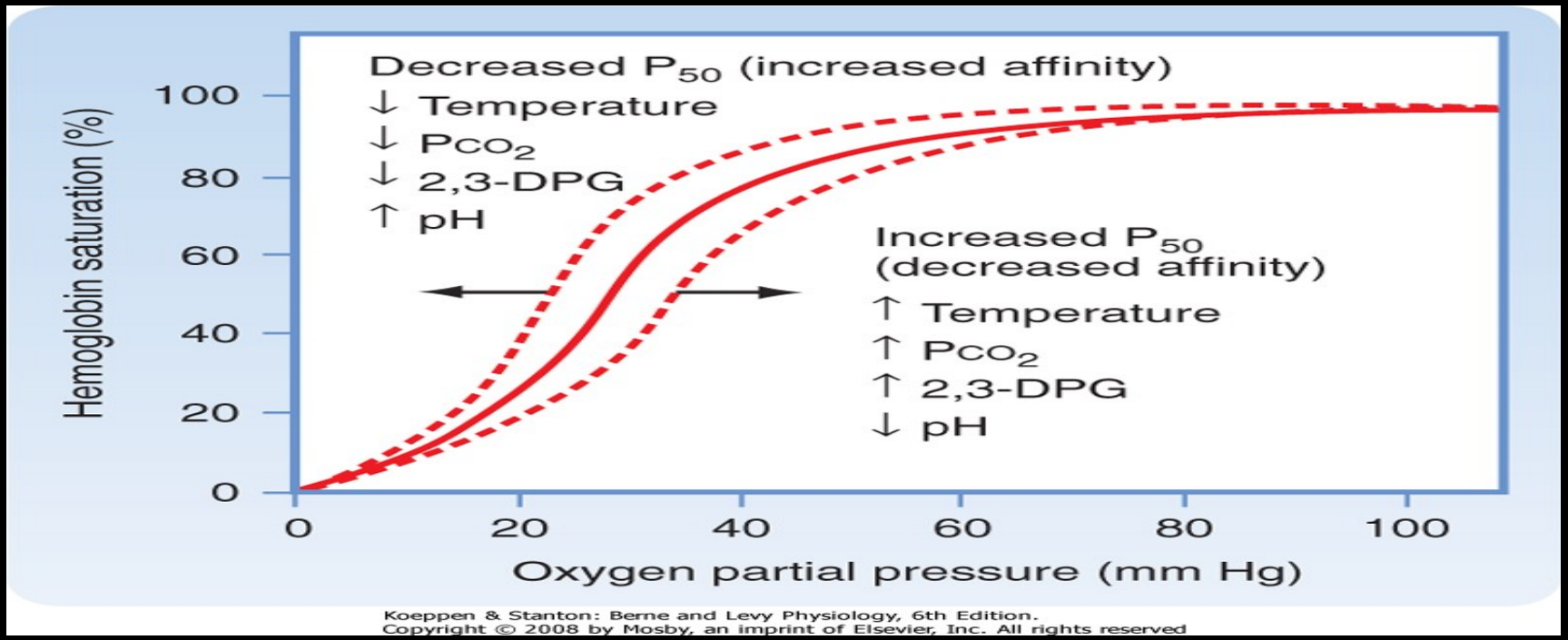
Oxygen – Haemoglobin Dissociation curve.



- As affinity of Hb for O2 **falls** graph shifted to **right**.
- As affinity of Hb for O2 **rise** graph shifted to **left**.
- H+ ion conc, Pco2 temp & 2,3-DPG affects shift.

Shift of Oxygen – Haemoglobin Dissociation curve.

- Shift to left.
- Shift to right.



VARIETIES OF HAEMOGLOBIN.

- **Physiological.**
- **Adult**
  - Haemoglobin A --

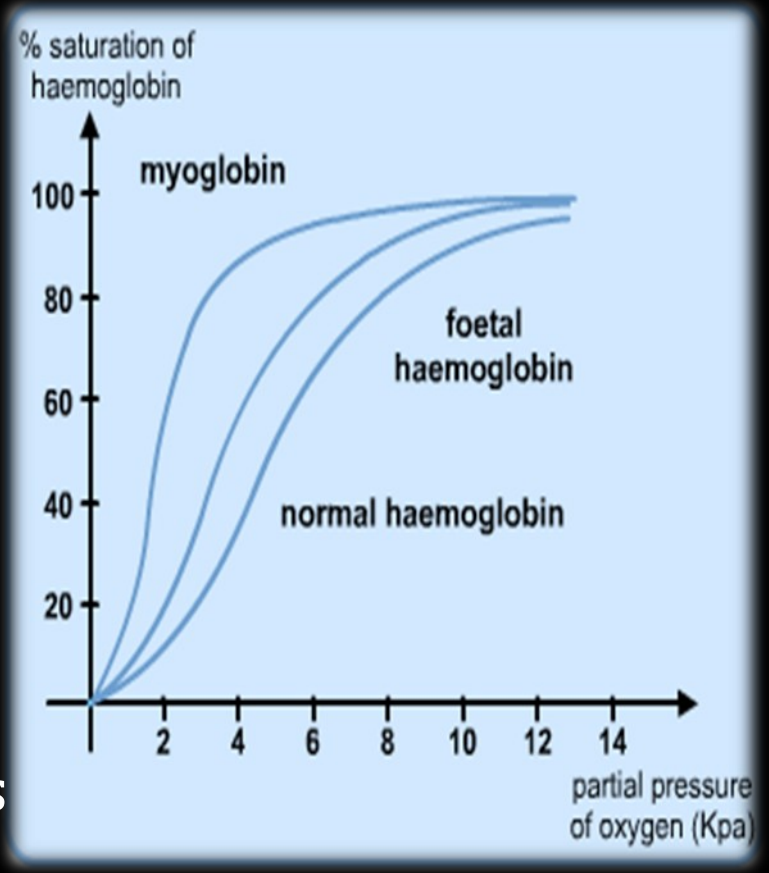
    4 polypeptide chains

    2 α (alpha) & 2 β (Beta)
  - Haemoglobin A2 -- 2 α (alpha) & 2 δ (Delta)
- **Fetal.**

- **Pathological** (Haemoglobinopathies)
  - Sickle Cell Haemoglobin.
  - Hb C
  - Thallasemia.

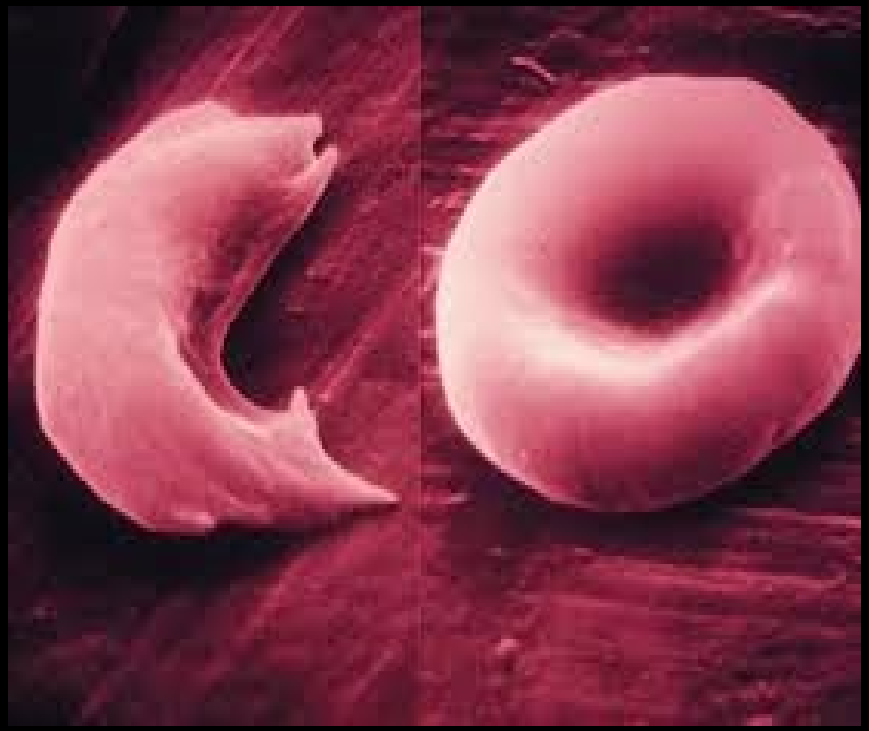
FETAL HAEMOGLOBIN.

- Present in fetal RBC & disappear in 2-3 months after birth.
- **Structure**
  - 4 polypeptide chains
    2 α(alpha) & 2 γ (gamma)
- **Characteristics.**
  - Affinity for oxygen – more
  - Resistance to action of alkalies
  - Life span – less.



PATHOLOGICAL (HAEMOGLOBINOPATHIES)

- **Sickle cell haemoglobin.(HbS)**
  - Substitution of **Valine** for **Glutamic Acid** at **6th** position in beta chain.
  - When HbS is reduced (in low O2 tension) precipitate into crystals in RBC changes shape become **Sickle shaped**.



EFFECTS OF SICKLE CELL SHAPE.

- **Less flexible** – blockage of microcirculation.
- **Increases blood viscosity.**
- **More fragile** – More Hemolysis – Anaemia.

TREATMENT

- **Drugs** – leads to formation of HbF which decreases polymerization of deoxygenated Hb.
  - Azacytidine
  - Hydroxyurea
- **Bone Marrow Transplantation.**

Pathological (Haemoglobinopathies)

- **Haemoglobin C.**
  - Similar to HbS but not associated with Sickling.
- **Other varieties are HbE, HbI, HbJ, HbM**
- **Thalassaemia**
  - Defect in synthesis of polypeptide chain.
  - Types
  - Major
  - Minor

DIFFERENCE IN THALASSAEMIA MAJOR & MINOR.

β Thalassaemia Major

- Less common
- Homozygous transmission
- Complete absence of beta chain synthesis.
- **Anemia** – moderate to severe
- **HbF** – markedly increased
- Life span – short
- **Cooley's Anaemia**

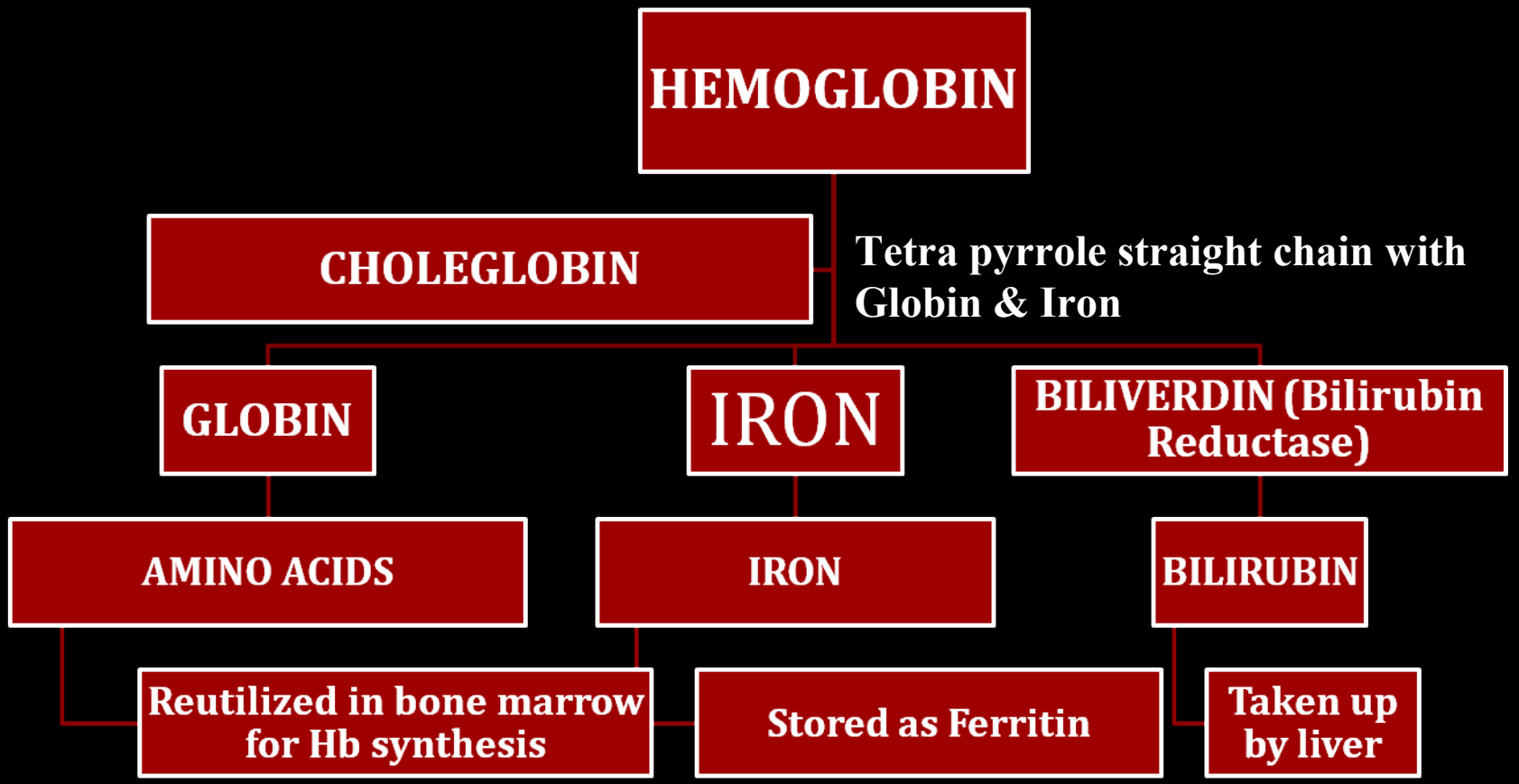
β Thalassaemia Minor.

- More common.
- Heterozygous transmission.
- Partial Absense.
- Anemia- mild.
- HbF – slightly elevated.
- Life span – comparatively longer.

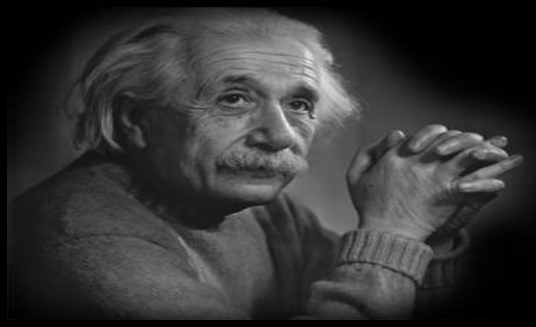
DERIVATIVES OF Hb

- 1. Hb + O_2 → HbO_2 (Oxyhaemoglobin) Iron in ferrous state)
- 2. Hb + Cyanide → Methaemoglobin Iron in ferric state.
- 3. Hb + CO_2 → Carbamino hemoglobin
- 4. Hb + CO → Carboxy hemoglobin
- 5. Hb + H_2S → Sulphemoglobin.
- 6. Hb + Glucose → Glycosylated (attached to terminal Valine)

FATE OF HAEMOGLOBIN



Education is what remains after one has forgotten what one has learned in school.



Albert Einstein
German Theoretical-Physicist
(1879-1955)

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THANK YOU