Haemoglobin.

Structure, Synthesis Functions & Degradation.

Haemoglobin is a respiratory pigment found in red blood corpuscles. Haemoglobin is a conjugated protein, synthesized inside immature erythrocyte in the red bone marrow.

It consists of two components Haem And Globin. Haem, an Iron and porphyrin compound is 4% and Globin (amino acids) is 96%.

Haemoglobin gives red colour to the blood.

Structure of Haemoglobin :-

In Haemoglobin A haem group consists of an iron (Fe) ion (charged atom) held in a heterocyclic ring, known as a porphyrin.

This porphyrin ring or protoporphyrin compound consists of four pyrrole molecules cyclically linked together by methane bridges.

The protoporphyrin compound combines with metal iron forming metalloporphyrin, where metal iron is 0.34%. Fe is in ferrous state.

The iron ion, which is the site of oxygen binding, coordinates with the four nitrogens in the center of the ring, which all lie in one plane.

3) The Globin of each Hb mole consist of a tetramers with two polypeptide chains of one kind & two of another. Globin helps heam to keep iron in ferrous state & combine loosely & reversibly with O2.
normal adult Hb i.e. in HbA-these chains are called α and β chains and HbA2 –α and δ chain are present. Each chain is composed of a sequence of about 150 amino acids. The substitution of any one these amino acids by another, results in formation of abnormal chain and abnormal Hb e.g. in Hb-S which is found in sickle cell anemia, glutamic acid( amino acid) is replaced by Valine, when exposed to hypoxic condition Hb-S produces long crystals called tactoid in the red cells.

Globin

Haem------ Iron ( Ferrous state)

Haem ------------

Protoporphyrin( 4 pyrrols)
Synthesis of Haemoglobin:

Synthesis of Haemoglobin begins at the erythroblast stage & continues through normoblast & reticulocyte. Synthesis occurs in the ribosome of endoplasmic reticulum.

Haem portion of Haemoglobin is synthesized in the following steps:

Formation of Haem

1) Acetic acid in Krebs cycle changes in to α- Keto glutaric acid which combines with Glycine to form Pyrrole compound.

2) 4 Pyrrole compounds combine to form Protoporphyrin III compound.

3) Protoporphyrin III + Fe -------- Haem (Metalloporphyrin)

Formation of Haemoglobin

4) 4 Haem + Globin -------- Haemoglobin

In adult humans, the most common haemoglobin type is a tetramer (which contains 4 subunit proteins) called haemoglobin A.

In Haemoglobin A, Globin is composed of 4 large polypeptide chains, consisting of two α and two β polypeptide chains (α₁ β₁ and α₂ β₂) non-covalently bound, each made of 141 and 146 amino acid residues, respectively. Abnormalities in the chain alter the physical characteristic of Hb.

Globin helps Haem to keep Fe in in ferrous state and combine loosely and reversibly with molecular oxygen.
Factors essential for the synthesis of Hb

1) First class proteins i.e. proteins of high biological value are necessary for Hb synthesis. e.g. Histidine, Phenyl alanine, Leucine etc.

2) Vitamins : Vit B12, Vit C are helpful in synthesis
   Folic acid, riboflavin, nicotinic acid, pantothenic acid play important role. Vit B12 and Folic acid are called maturation factors and are required for multiplication and maturation of RBC.

3) Endocrine Secretions : Thyroid hormones are required for synthesis.
   Thyroxine is important.

4) It is required in ferrous state for synthesis of the haem of Hb and deficiency of Fe causes microcytic and hypocromic anemia. Adult requirement is 10- 20 mg /day

5) Copper is required for biosynthesis of Hb.

6) Cobalt and Manganese is required in very small quantities.

Normal Level of Haemoglobin in Human Body

Amount of Hb in normal Blood irrespective of Sex is 14.5 g/% (by Sahlis method)

Normal Hb level in Males 14-17 gm/% (gms per 100 ml)

Normal Hb level in Females 12-15 gm/% (gms per 100 ml)

Age, sex, diurnal variation, altitude, exercise, excitement, adrenaline affects the Hb level.

Functions of Haemoglobin
**Oxygen carriage:** The most important function of Hb is to carry Oxygen to the tissues and carry co₂ away from the tissues to the lungs. When fully saturated, each gram of Hb holds approximately 1.34 ml of O₂.

Hb combines loosely and reversibly with O₂ in the lungs where O₂ tension is high forming **oxy-haemoglobin** (Hb O₂). It is an unstable compound and can give up O₂ in tissue capillaries where O₂ tension is very low.

**Transport of CO₂:** Globin part of Hb combines with CO₂ and forms carbamino compound. Enzyme carbonic dehydrogenase helps in this transport.

**Hb as buffer:** Hb constitutes one of the important buffer of the blood and helps to maintain its acid–base balance.

**Hb has a strong tendency to combine with carbon monoxide** forming a compound called carboxyhaemoglobin. CO has almost 250 times stronger affinity for Hb than that of O₂ for Hb. CO-Hb once formed in the blood prevents formation of oxyhaemoglobin leading to hypoxia.

**Various pigments of bile, stool and urine are formed from Hb.**

**Release and Degradation of haemoglobin:** As RBCs become old and senile, they change their shape, size and become more brittle. They throw out processes called pseudopodia later on processes are broken and RBCs disintegrate. Fragmentation takes place in the circulation and fragments are swallowed by the cells of reticulo endothelial system of spleen and liver, Hb is released from RBC and later on degraded.

When Hb undergoes degradation:

1) Porphyrin rings open and four pyrrole groups form chain instead of ring,
2) The degraded product is called Verdohaemoglobin or Choleglobin.
3) From this Haem and Globins are separated.
4) From globin amino acids are separated.

5) **From haem**, iron is separated and carried as **transferrin** either to bone marrow for production of new RBC or to liver and other tissues for storage in the form of **ferritin** and **haemosiderin**.

6) The rest of haem molecule is converted into a yellow pigment **bilirubin** which is oxidised to a green pigment **biliverdin**.

7) Bilirubin and biliverdin combine with plasma α₁-globulin, circulate through blood and enter the liver.

8) In liver cells, Bilirubin and biliverdin separated from plasma α₁-globulin and conjugate with **Uridine diphosphate glucuronate** and form **monobilirubin** and **dibilirubin glucuronide**.

9) These compounds enter the **duodenum** through bile duct and then pass to the large intestine.

10) In large intestine by **bacterial action** they are changed into **Stercobilinogen**

11) Some Urobilinogen is reabsorbed and excreted in urine as **urobilin**

12) The rest is excreted in the faeces as Stercobilinogen and stercobilin which gives brown colour to stool.