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Zoology – II

Haematology

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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. In

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 ($\alpha_1 \beta_1$ and $\alpha_2 \beta_2$) 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, Phynyl 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 hypochromic 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 CO_2 away from the tissues to the lungs. When fully saturated, **each gram of Hb holds approximately 1.34 ml of O_2 .**

Hb combines loosely and reversibly with O_2 in the lungs where O_2 tension is high forming **oxy-haemoglobin**

(Hb O_2). It is an unstable compound and can give up O_2 in tissue capillaries where O_2 tension is very low.

Transport of CO_2 : Globin part of Hb combines with CO_2 and form carbamino compound. Enzyme carbonic dehydrogenase helps in this transport.

Hb as buffer : Hb constitute 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 O_2 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 oxydised to a green pigment **biliverdin**.
- 7) **Bilirubin and biliverdin** combine with **plasma α_1 – globulin** , circulate through blood and enter the liver.
- 8) **In liver cells, Bilirubin and biliverdin** separated from **plasma α_1 – globulin** and conjugate with **Uridine diphosphate glucuronate** and form **monobilirubin and Dibilirubin glucuronide**.
- 9) These compounds enter the **deuodenum** 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.