UG SEM-IV
CC-9T: Animal Physiology:Life Sustaining Systems
Unit 3: Physiology of Circulation

Structure & Function of

Haemoglobin

SANJIB KR. DAS
ASST. PROFESSOR
DEPT. OF ZOOLOGY
JHARGRAM RAJ COLLEGE

Structure of haemoglobin

- Mol. Wt 68000
- Globin (protein) + Haem (iron containing pigment)
- Globin part of HbA consists of

  2 α chains- 141 aa- chr-16

  2 β chains- 146 aa – chr- 11

- Haem part consists of **Porphyrin nucleus** and **Iron**

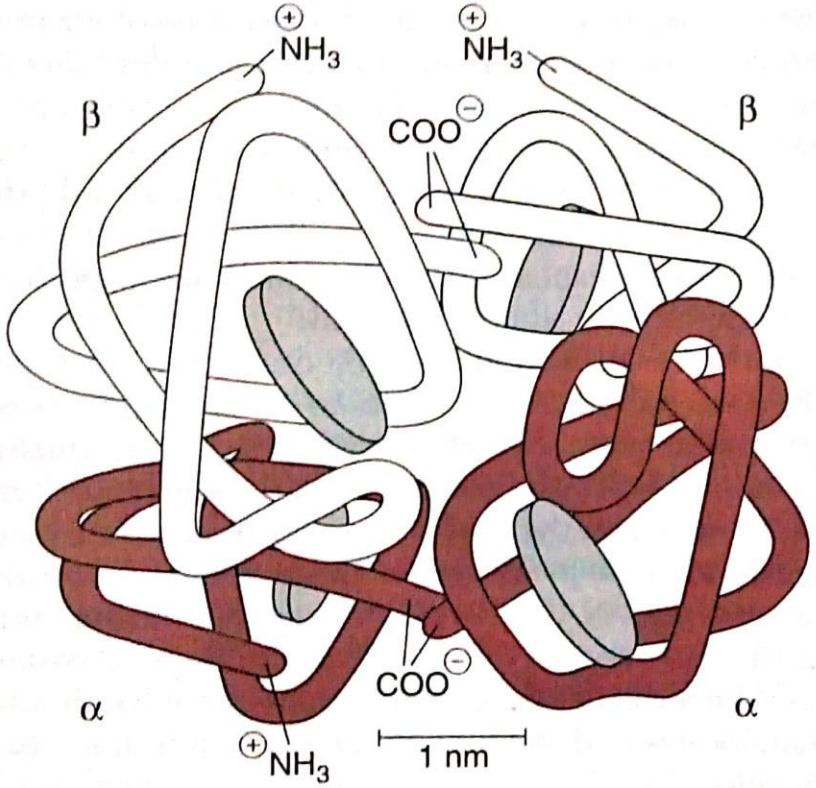


Figure 27–17 Diagrammatic representation of a molecule of hemoglobin A, showing the four subunits. There are two α and two β polypeptide chains, each containing a heme moiety. These moieties are represented by the disks. (Reproduced, with permission, from Harper HA et al: *Physiologische Chemie.* Springer, 1975.)

Porphyrin nucleus:

- Tetra pyrroles- I,II,III,IV
- Pyrrole rings are joined together by 4 methine bridges (=CH-)
- Carbon atoms of =CH- are, α, β, γ, δ
- Side chains of Pyrrole rings
- 4 methyl (1, 3, 5, 8)
- 2 vinyl (2, 4)
- 2 propionic acid (6, 7)

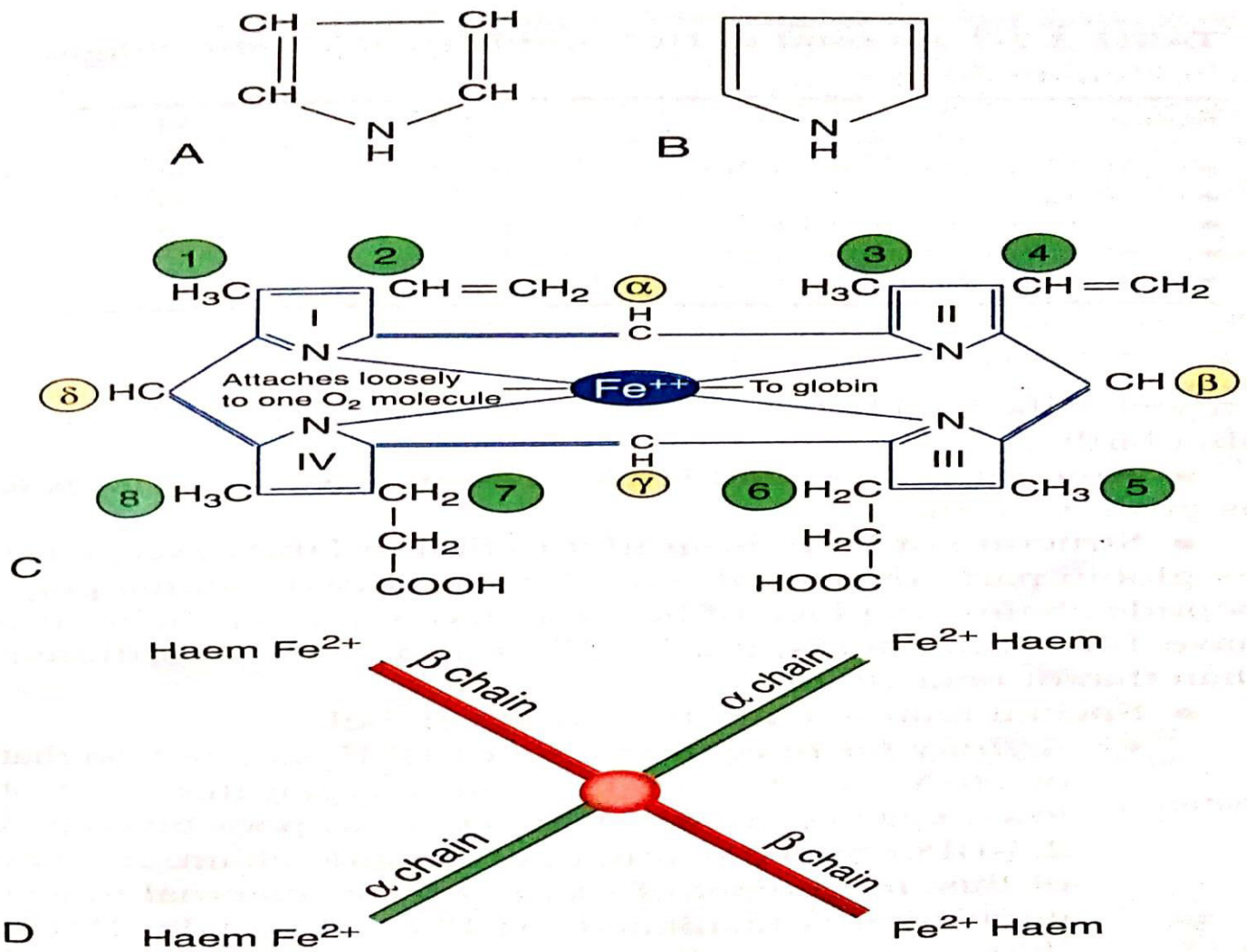


FIGURE 3.2-16 Chemistry of haemoglobin: **A,** structure of a pyrrole ring; **B,** conventional outline of a pyrrole ring; **C,** arrangement of pyrrole rings in one unit of haem (iron protoporphyrin X); and **D,** arrangement of four units of haem in one molecule of haemoglobin.

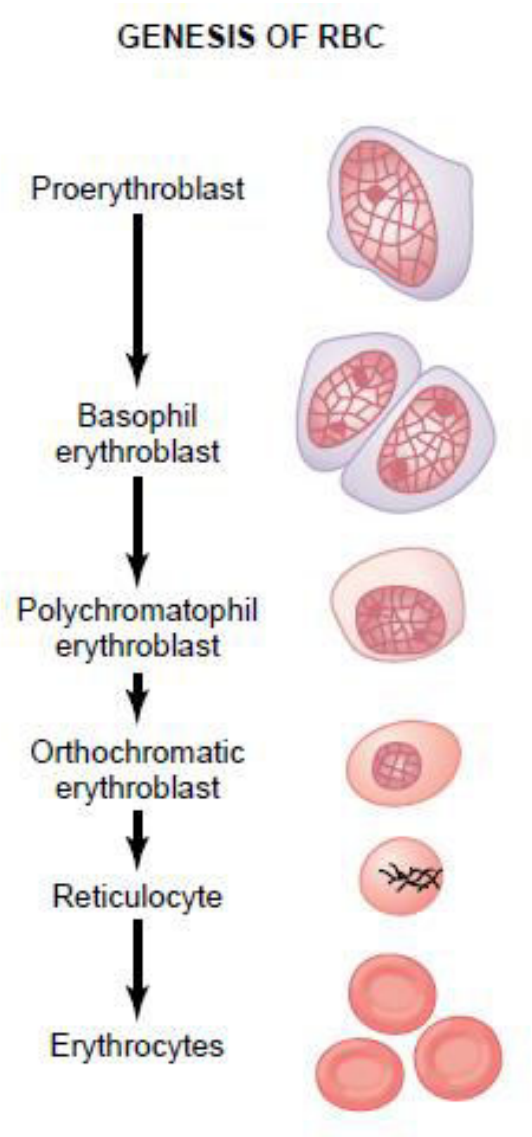
The iron:

- In Ferrous form Fe++
- Attached to the 4 N atom of pyrrole ring
- Attached loosely to one O2 molecule
- Attached to globin chain

- Attachment of Haem to Globlin
- 1 molecule of Hb consists of 4 units of Haem
- Each Haem binds to 1 of 4 polypeptide chains
- 4 Iron atoms can carry 4 molecule (8 atoms) of oxygen.
- HbO_2 Hb_2O_4 Hb_3O_6 Hb_4O_8

Formation of Hemoglobin

- Synthesis of hemoglobin begins in the proerythroblasts and continues even into the reticulocyte stage of the red blood cells. Therefore, when reticulocytes leave the bone marrow and pass into the blood stream, they continue to form minute quantities of hemoglobin for another day or so until they become mature erythrocytes.



Development of haemoglobin in human

- First appear at about 6 weeks after gestation
- Embryonic Hb Portland

  Hb Gower I

  Hb Gower II ($\alpha_2\epsilon_2$)
- 10-11 weeks HbF ($\alpha_2\gamma_2$) becomes prominent
- At 38 weeks HbA ($\alpha_2\beta_2$) synthesis starts

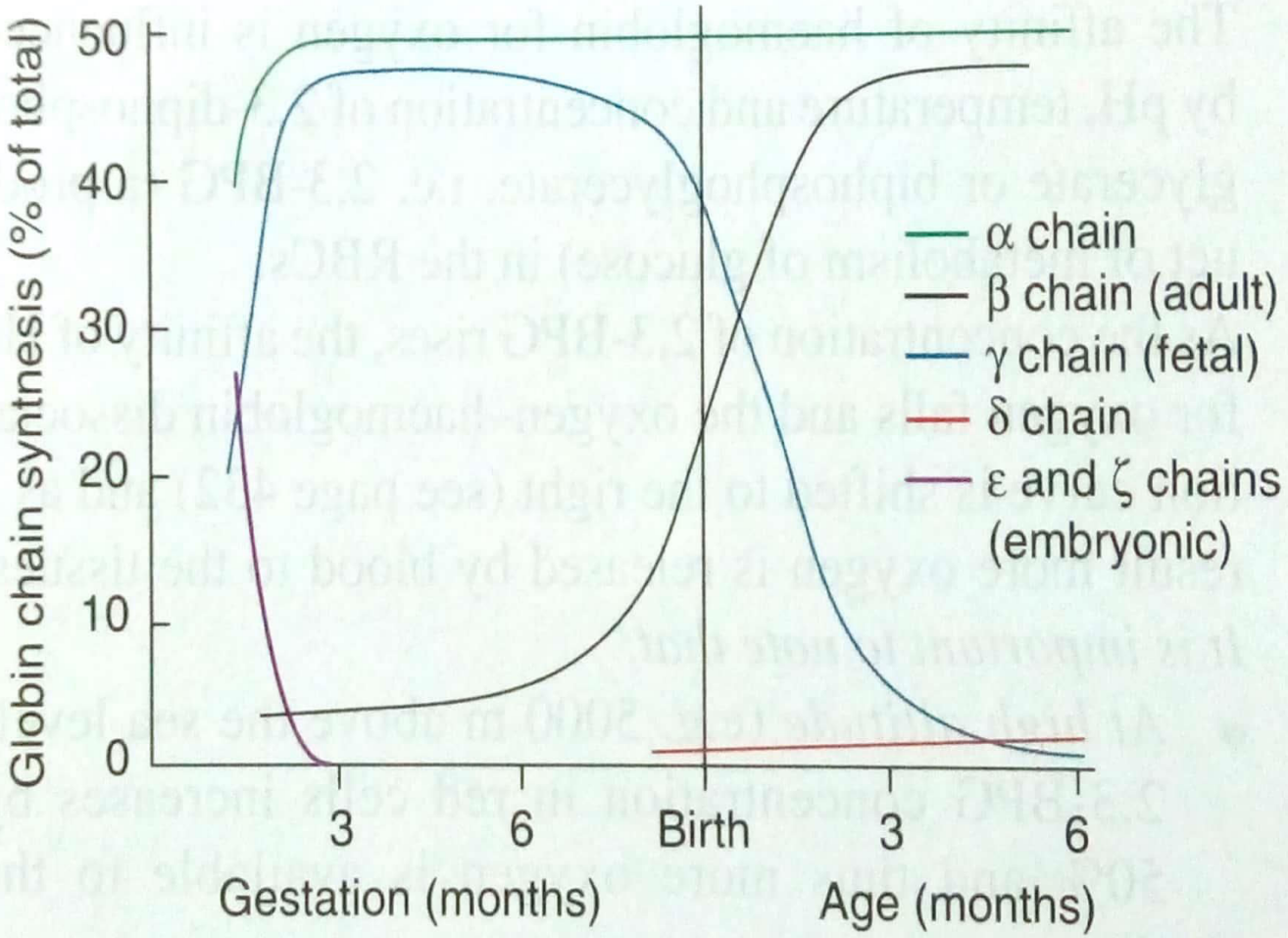


FIGURE 3.2-17 Development of human haemoglobin chains.

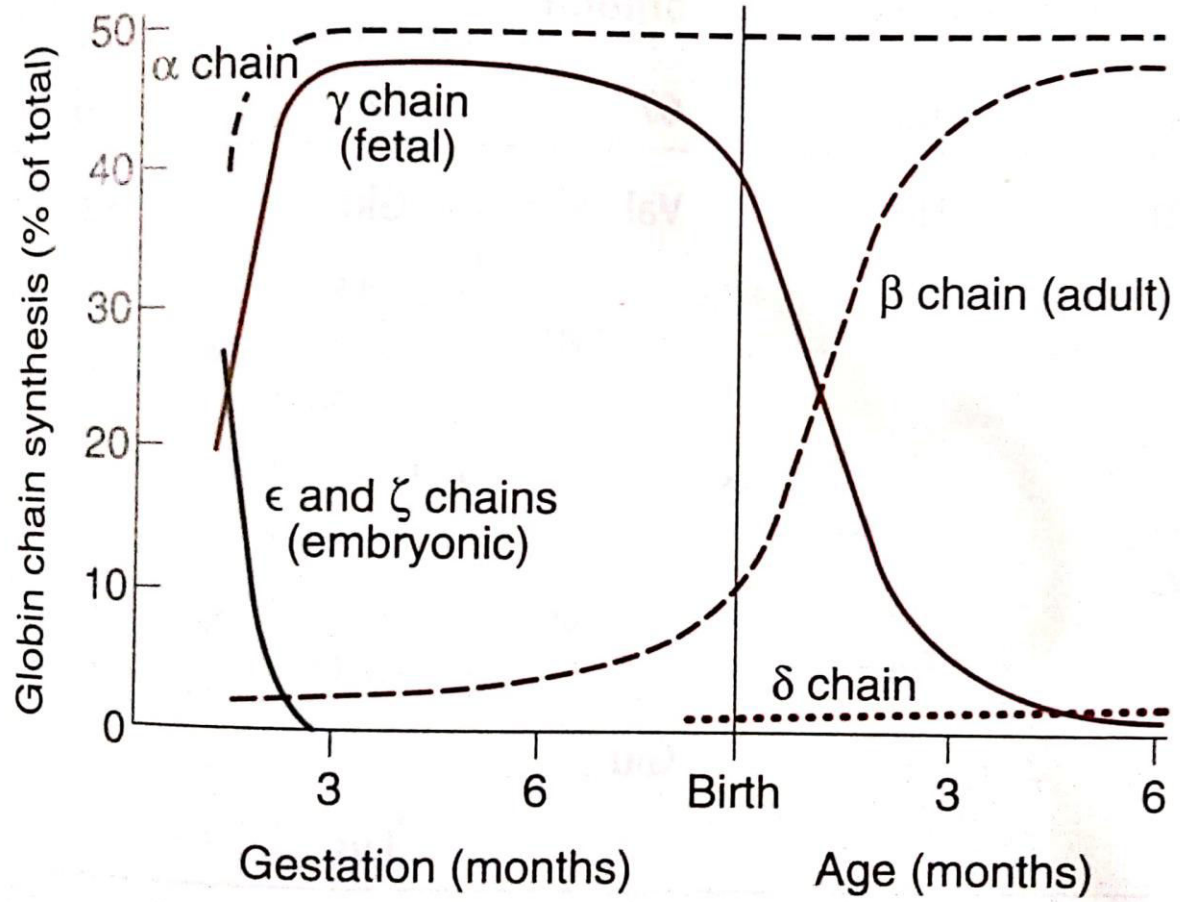
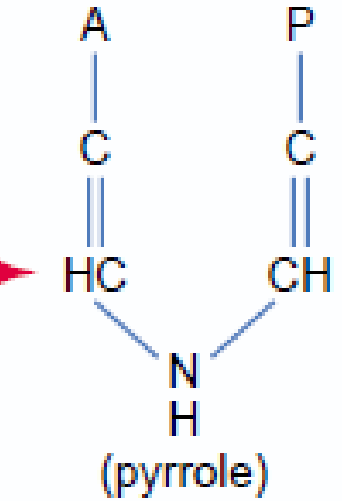


Figure 27–19 Development of human hemoglobin chains.

TABLE 3.2-3 Amount of HbF and HbA at Various Stages in Human Beings

Stage	HbF	HbA
• At 20 weeks of intrauterine	94%	6%
• At birth	80%	20%
• At 2 months after birth	50%	50%
• At 4 months after birth	10%	90%
• At more than 1 year after birth	<1%	>99%

I. 2 succinyl-CoA + 2 glycine → 

(pyrrole)

II. 4 pyrrole → protoporphyrin IX

III. protoporphyrin IX + Fe^{++} → heme

IV. heme + polypeptide → hemoglobin chain (α or β)

V. 2 α chains + 2 β chains → hemoglobin A

Formation of hemoglobin.

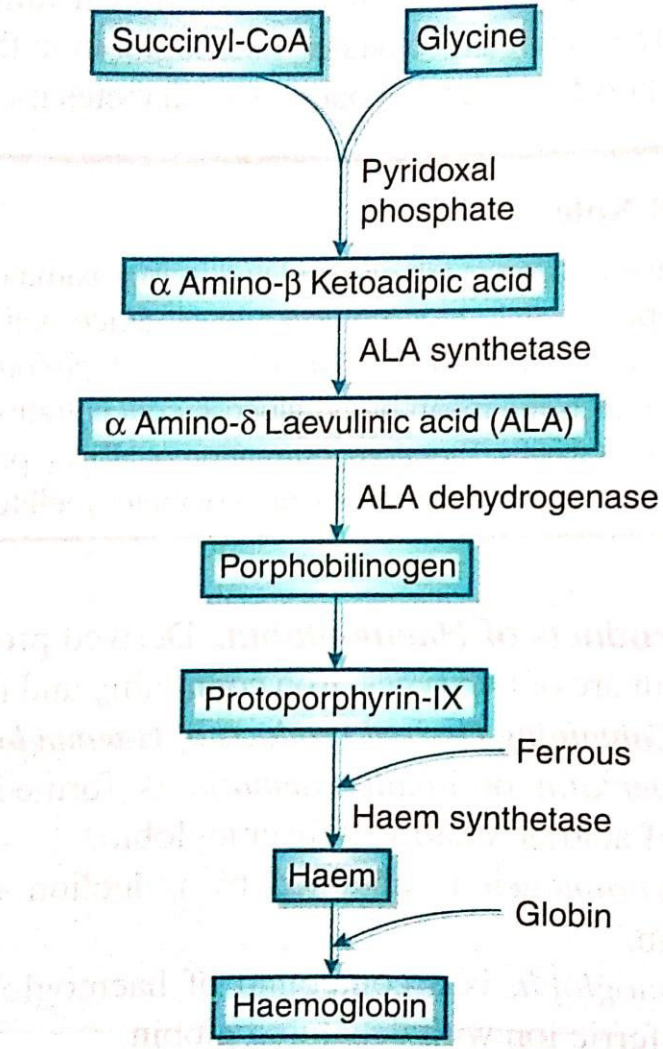


FIGURE 3.2-20 Steps of synthesis of haemoglobin.

FUNCTIONS OF HAEMOGLOBIN

- Transport of O_2 from Lungs to Tissues
- Transport of CO_2 from the Tissues to the Lungs
- Control pH of the blood

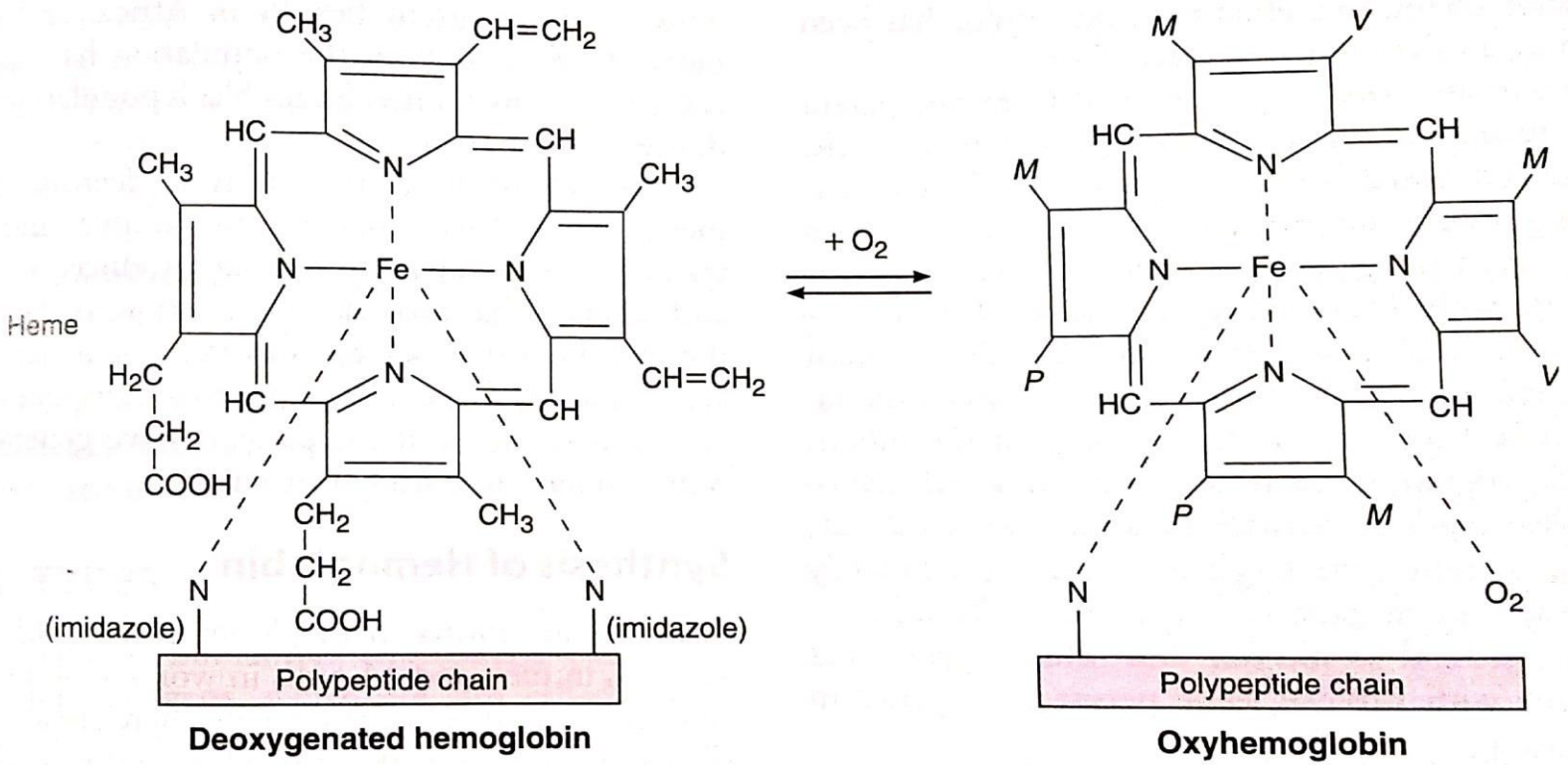
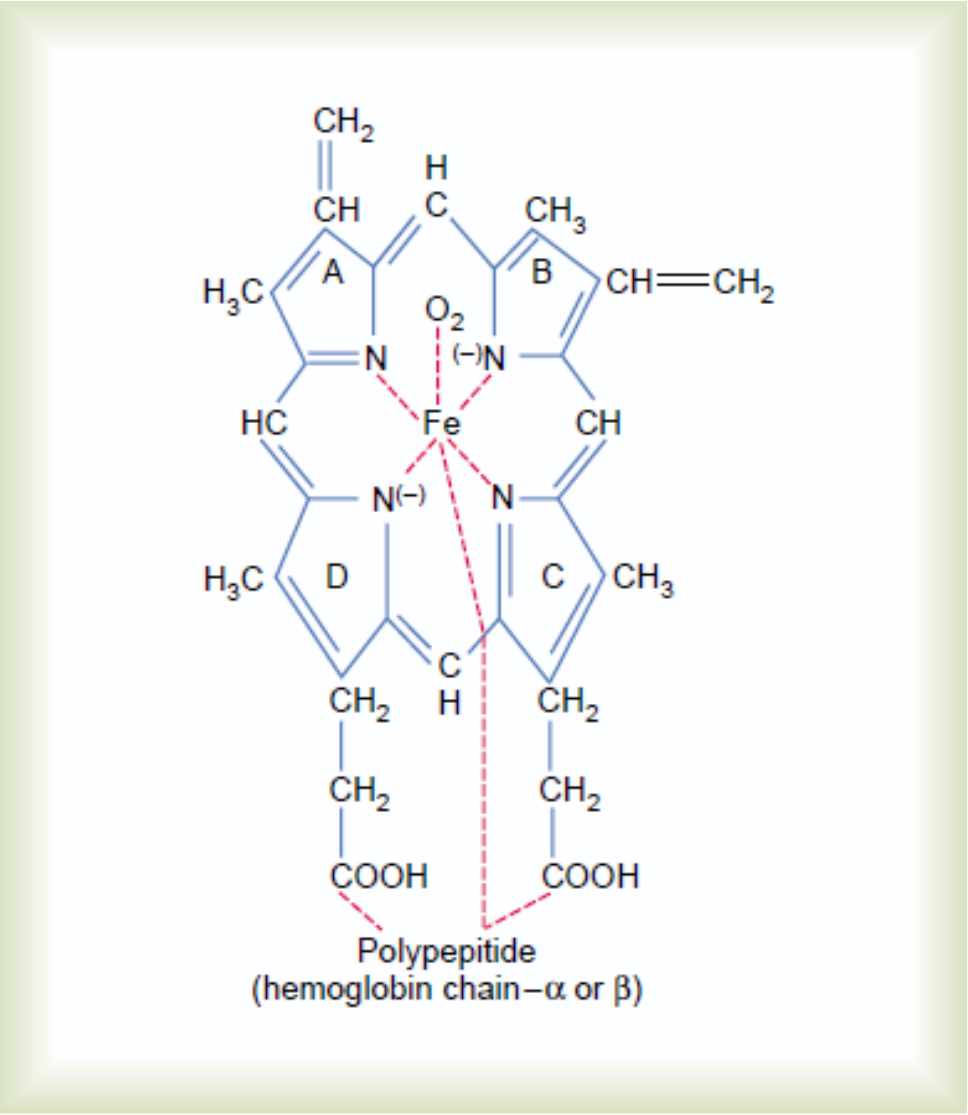


Figure 27–18 Reaction of heme with O_2. The abbreviations M, V, and P stand for the groups shown on the molecule on the left.



Basic structure of the hemoglobin molecule, showing one of the four heme chains that bind together to form the hemoglobin molecule.

- Oxygen does not combine with the two positive bonds of the iron in the hemoglobin molecule. Instead, it binds loosely with one of the so-called coordination bonds of the iron atom. This is an extremely loose bond, so that the combination is easily reversible.
- Furthermore, the oxygen does not become ionic oxygen but is carried as molecular oxygen (composed of two oxygen atoms) to the tissues, where, because of the loose, readily reversible combination, it is released into the tissue fluids still in the form of molecular oxygen rather than ionic oxygen.

Derivatives of haemoglobin:

- Oxyhaemoglobin
- Carbamino-haemoglobin
- Carboxy haemoglobin
- Methaemoglobin
- Sulphaemoglobin
- Nitrous Oxide Haemoglobin
- Glycosylated Haemoglobin

DERIVED PRODUCTS OF HAEMOGLOBIN

- Iron containing derived products of Hb
  - Acid/alkali haematin
  - Haemochromogen
  - Cathaemoglobin
  - Haem
- Iron-Free derived products of Hb
  - Haematoporphyrin
  - Haempyrrole
  - Haematoidin
  - Bilirubin

Destruction of Hemoglobin.

- When red blood cells burst and release their hemoglobin, the hemoglobin is phagocytized almost immediately by macrophages in many parts of the body, but especially by the Kupffer cells of the liver and macrophages of the spleen and bone marrow.
- During the next few hours to days, the macrophages release iron from the hemoglobin and pass it back into the blood, to be carried by transferrin either to the bone marrow for the production of new red blood cells or to the liver and other tissues for storage in the form of ferritin.
- The porphyrin portion of the hemoglobin molecule is converted by the macrophages, through a series of stages, into the bile pigment *bilirubin, which is released into the blood and* later removed from the body by secretion through the liver into the bile

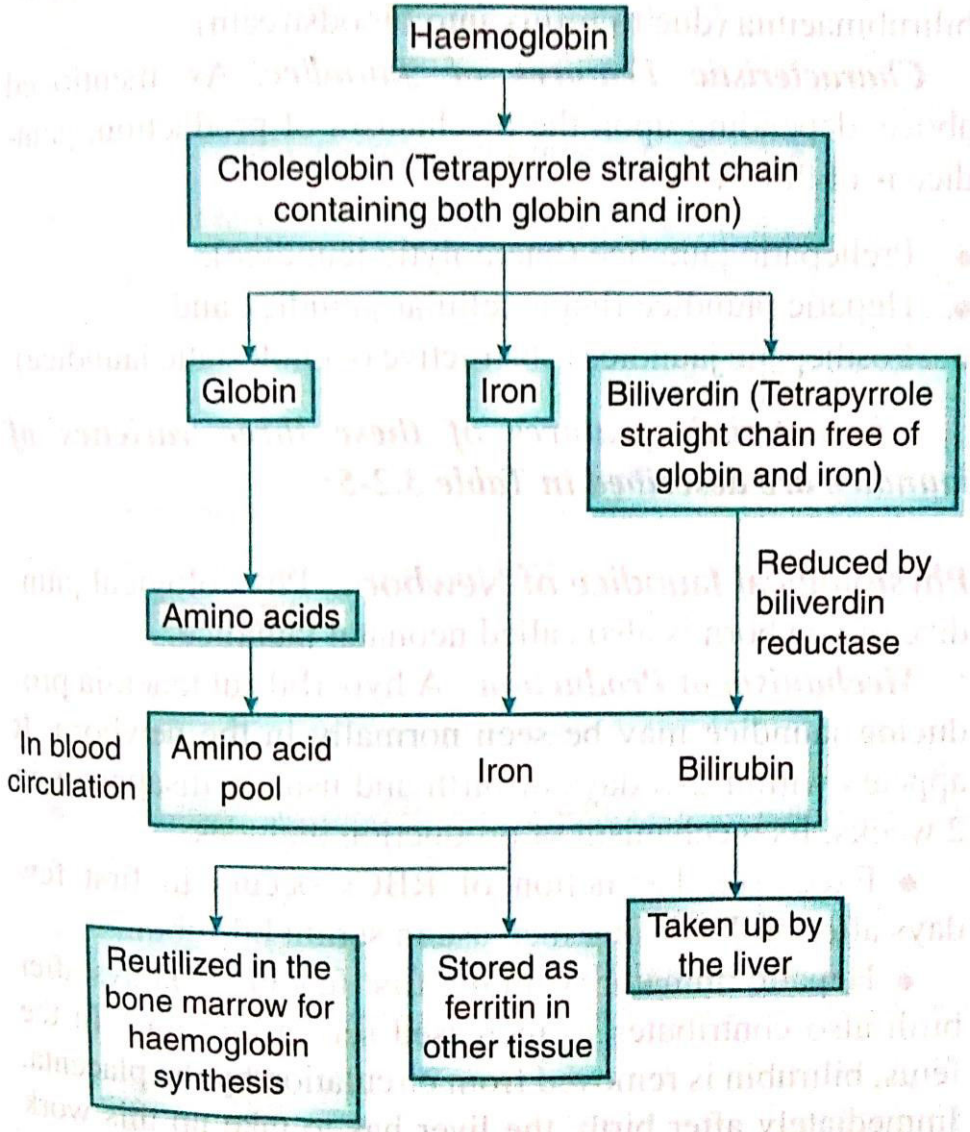
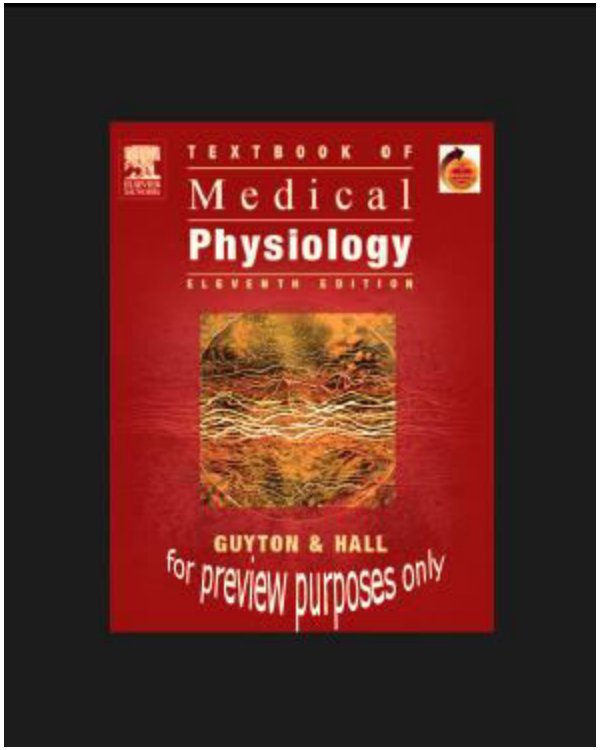


FIGURE 3.2-22 Fate of haemoglobin.

Reference: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