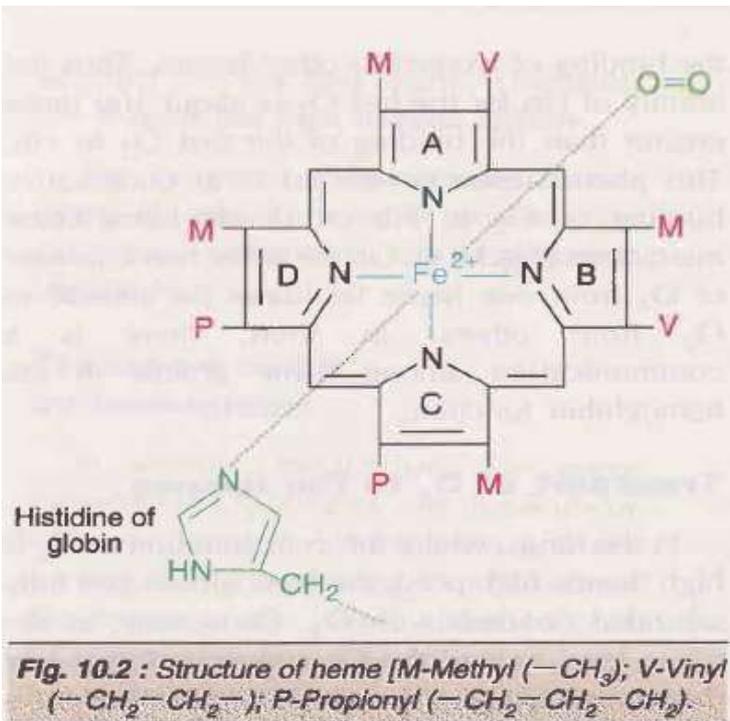
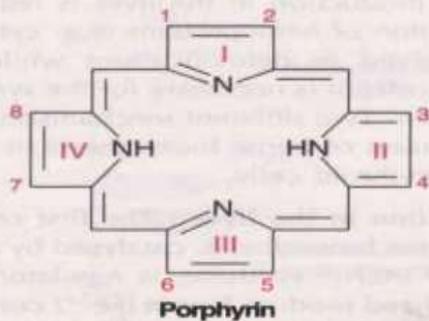
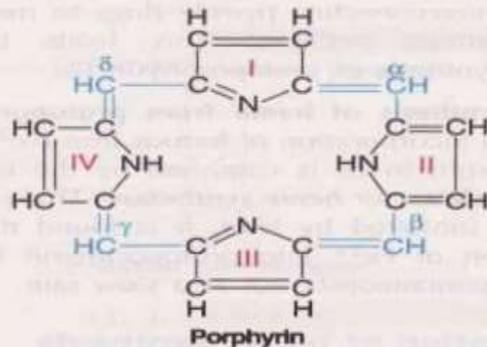
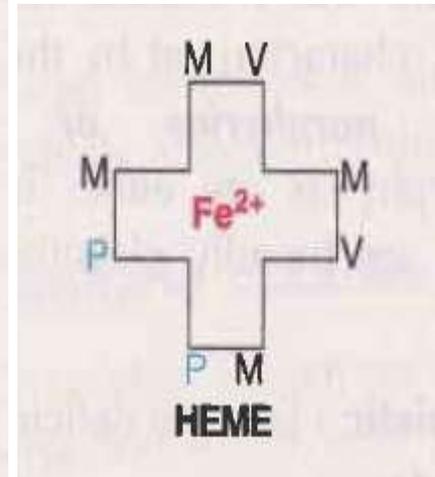


# Catabolism of Heme

- Heme is the **non-protein part of Hemoglobin**.
- Heme is the most important **porphyrin** containing compound.
- Porphyrins are cyclic compounds composed of 4 pyrrole rings held together by methenyl(=CH) bridges.
- It is synthesized in the **liver and bone marrow**.



**Fig. 10.2 :** Structure of heme [M-Methyl ( $-CH_3$ ); V-Vinyl ( $-CH_2-CH_2-$ ); P-Propionyl ( $-CH_2-CH_2-CH_2-$ ).



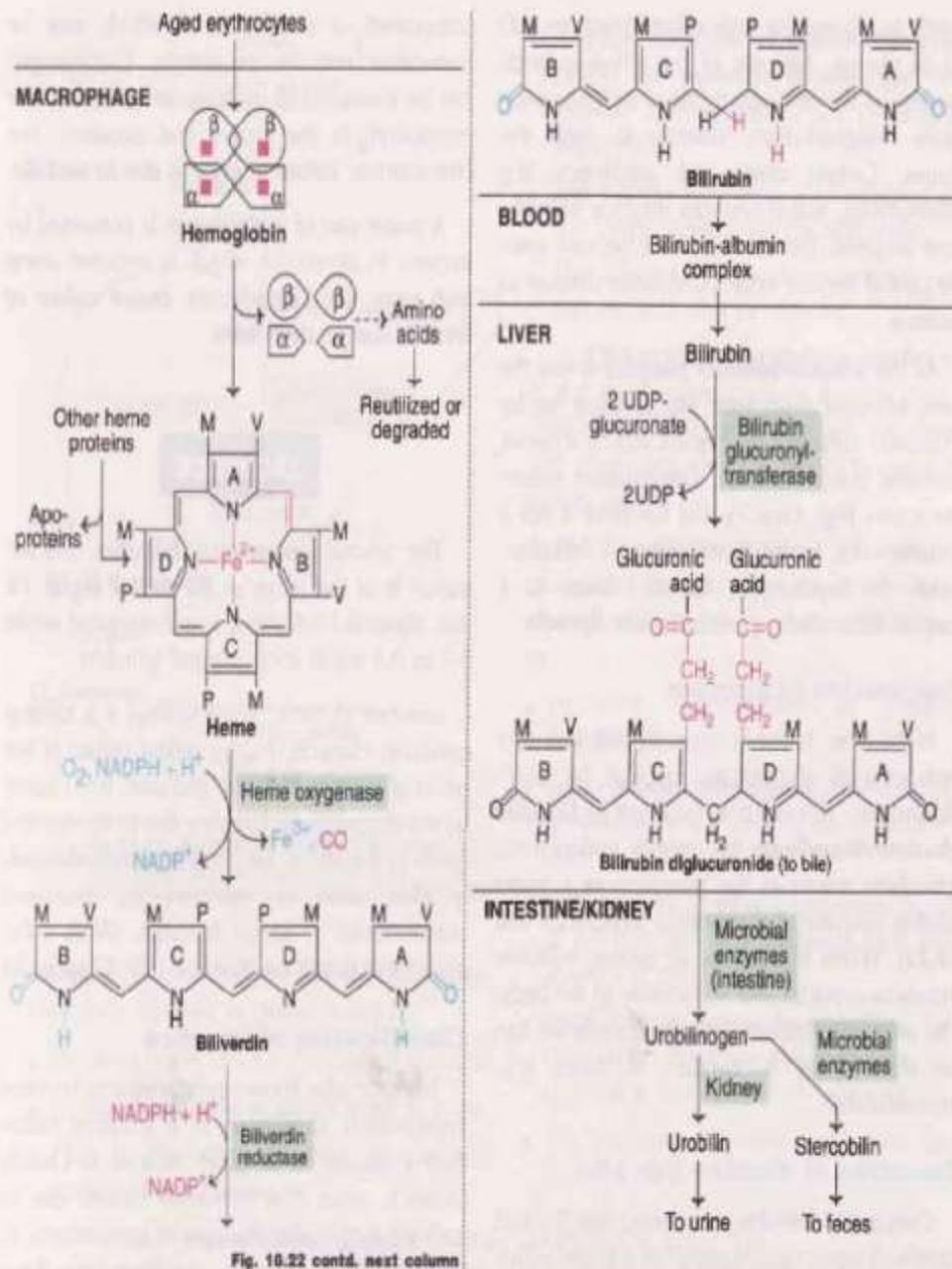


Fig. 10.22 contd. next column

Fig. 10.22 : Degradation of heme to bile pigments

(Note : Colours used in structures represent change in the specific reaction only.)

- **Heme oxygenase** utilizes NADPH and O<sub>2</sub> and cleaves the methenyl bridges between the two pyrrole rings (A and B) to form biliverdin.
- Simultaneously, ferrous iron (Fe<sup>2+</sup>) is oxidized to ferric form (Fe<sup>3+</sup>) and released.
- The products of heme oxygenase reaction are **biliverdin** (a green pigment), **Fe<sup>3+</sup>** and **carbon monoxide (CO)**.
- Biliverdin's methenyl bridges (between the pyrrole rings C and D) are reduced to form **bilirubin** (yellow pigment).
- This reaction is catalysed by **biliverdin reductase**.
- **Transport of bilirubin to liver** : Bilirubin is lipophilic and therefore insoluble in aqueous solution. So it is non covalently bound to albumin and is transported.

# Hyperbilirubinemia and Jaundice

- **Hyperbilirubinemia** represent the increased concentration of serum bilirubin.
- **Jaundice** is a clinical condition characterized by **yellow colour** of the white of the eyes (sclerae) and skin.
- This is due to the **elevated serum bilirubin level, usually beyond 2 mg/dl (normal < 1 mg/dl)**.
- **Hemolytic jaundice** : is associated with increased hemolysis of erythrocytes
- In hemolytic jaundice, more bilirubin is excreted into the bile.
- Hemolytic jaundice is characterized by:
  1. Elevation in the serum unconjugated bilirubin.
  2. Increased excretion of urobilinogen in urine.
  3. Dark brown colour of feces

- 
- Hepatic (hepatocellular) jaundice is caused by dysfunction of the liver due to damage to the parenchymal cells.
  - Hepatic jaundice is characterized by
    1. Increased levels of conjugated and unconjugated bilirubin in the serum.
    2. Dark coloured urine.
    3. Increased activities of alanine transaminase (SGPT) and aspartate transaminase (SCOT) released into circulation due to damage to hepatocytes.
    4. The patients pass pale, clay coloured stools.
    5. Nausea and anorexia (loss of appetite)
  - Obstructive (regurgitation) jaundice is due to an obstruction in the bile duct that prevents the passage of bile into the intestine.
  - Obstructive jaundice is characterized by:
    1. Increased concentration of conjugated bilirubin in serum.
    2. Serum alkaline phosphatase is elevated
    3. Dark coloured urine.
    4. Feces contain excess fat
    5. nausea and gastrointestinal pain