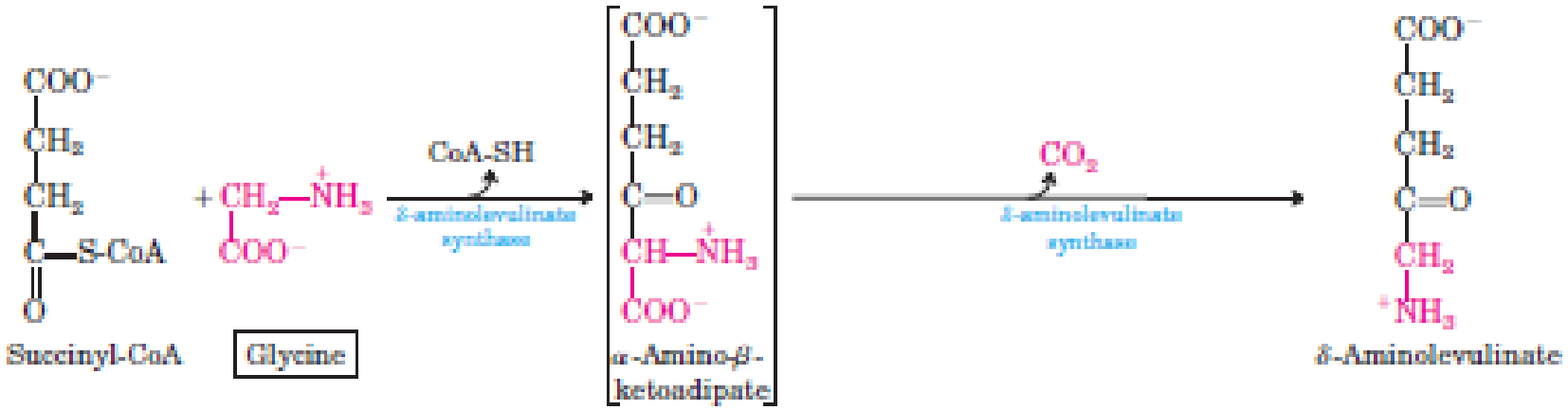
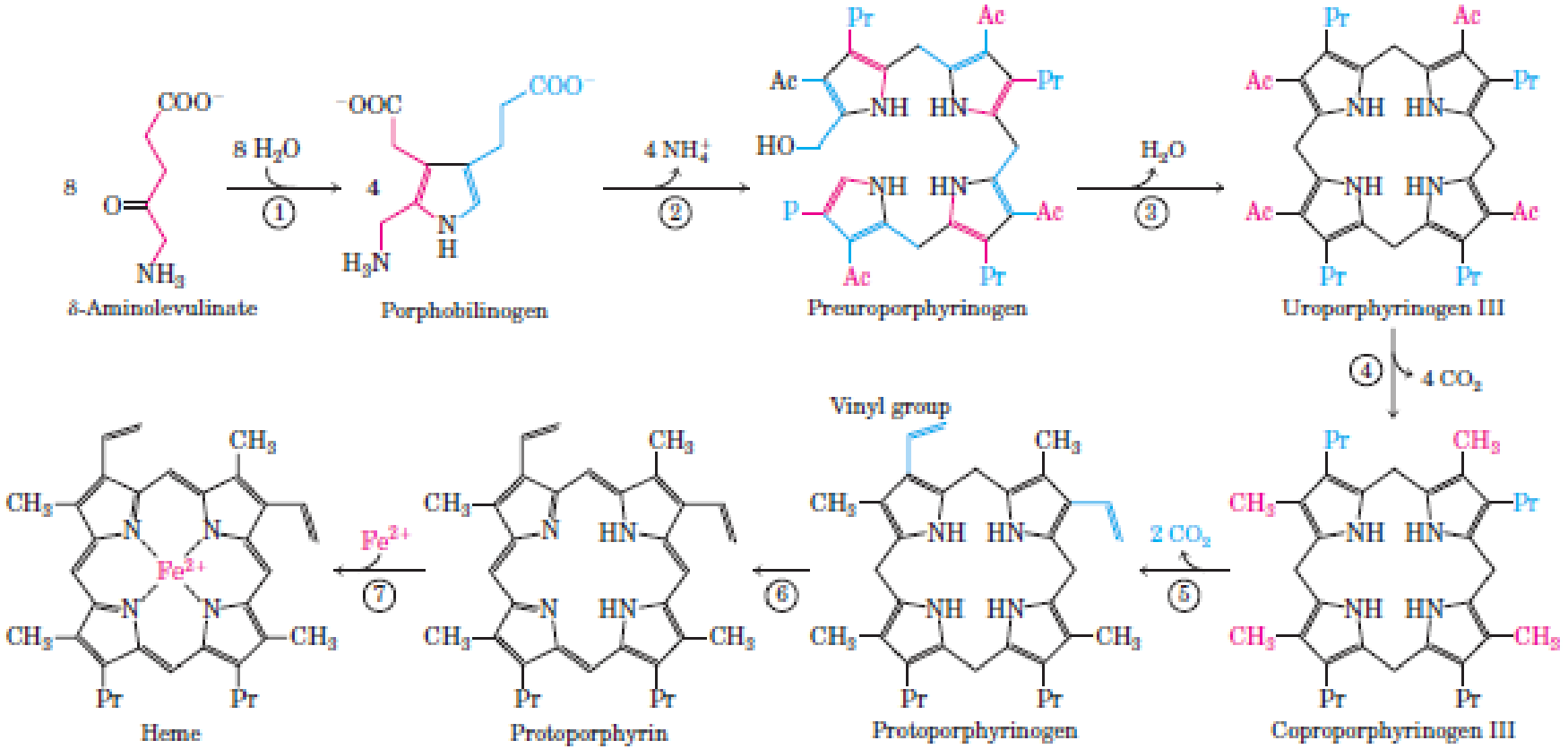
BIOSYNTHESIS AND CATABOLISM OF PORPHYRINS



Biosynthesis of δ–aminolevulinate

In mammals and other higher eukaryotes, δ-aminolevulinate is synthesized from glycine and succinyl-CoA. The atoms furnished by glycine are shown in red.

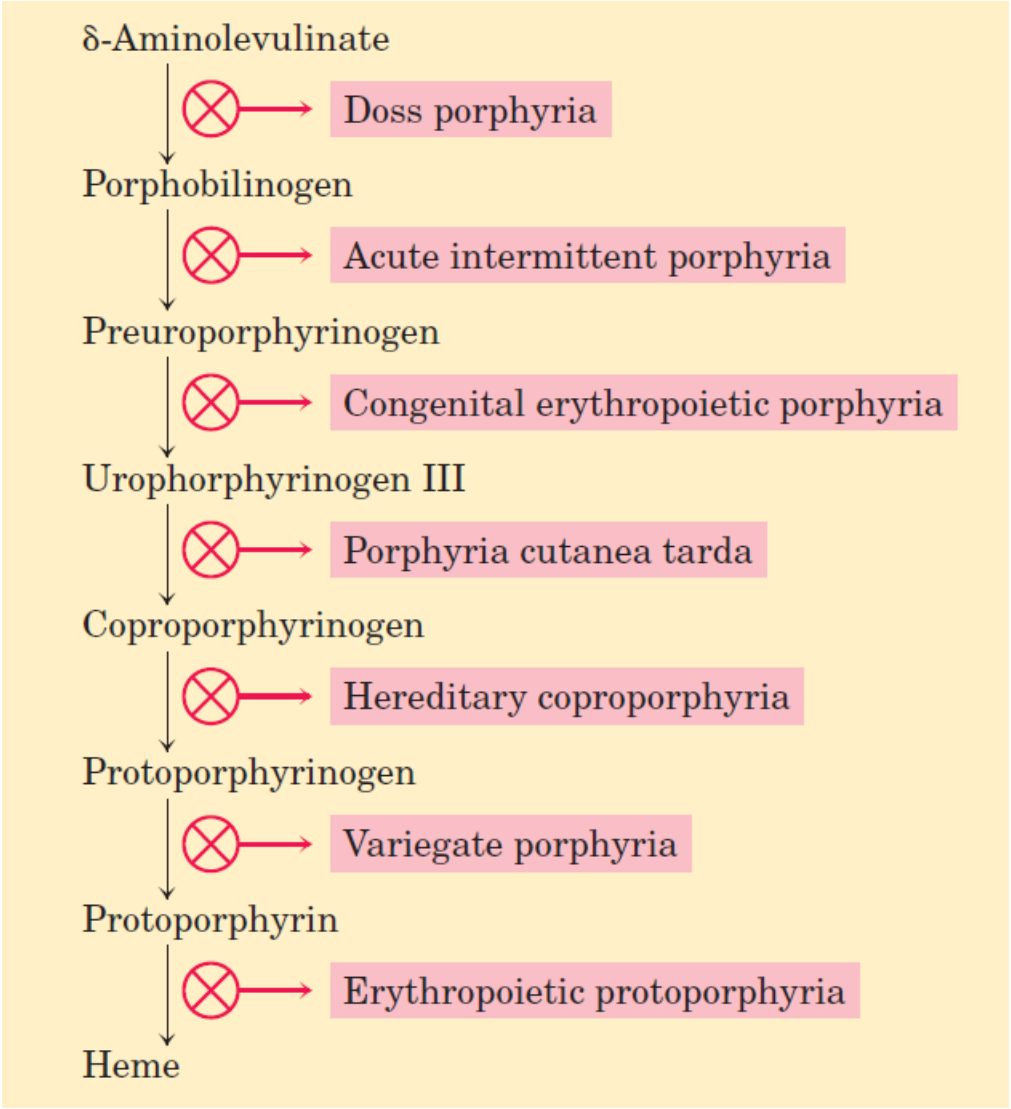


Biosynthesis of heme from δ-aminolevulinate

Ac represents acetyl ($-CH_2COO^-$); Pr, propionyl ($-CH_2CH_2COO^-$).

Porphyrias are a group of genetic diseases in which, because of defects in enzymes of the biosynthetic pathway from glycine to porphyrins, specific porphyrin precursors accumulate in erythrocytes, body fluids, and the liver. The most common form is acute intermittent porphyria. Most affected individuals are heterozygotes and are usually asymptomatic, because the single copy of the normal gene provides a sufficient level of enzyme function.

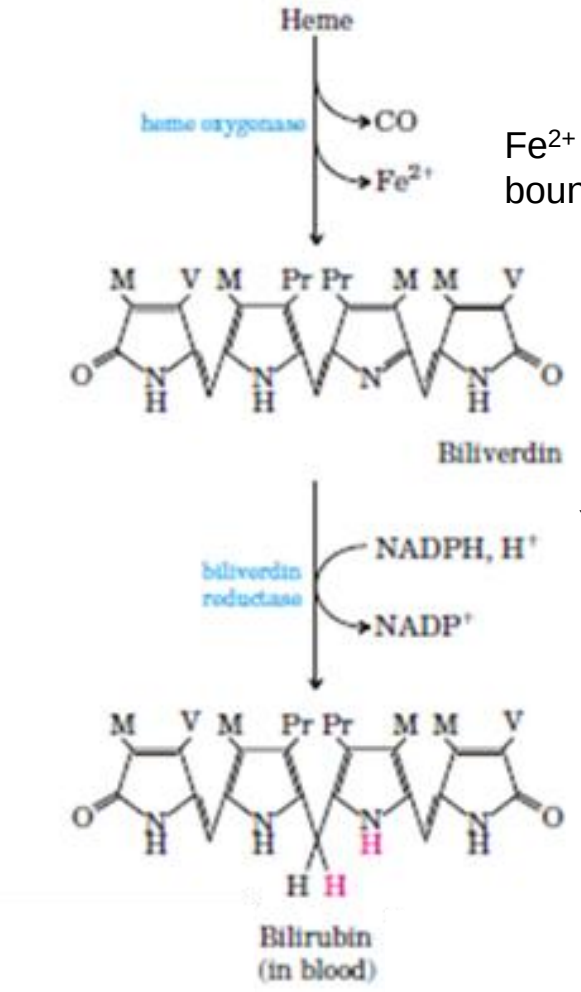
More severe conditions can cause a buildup of δ–aminolevulinate and porphobilinogen, leading to attacks of acute abdominal pain and neurological dysfunction.



Bilirubin and its breakdown products

M, methyl;
V, vinyl;
Pr, propionyl;
E, ethyl.

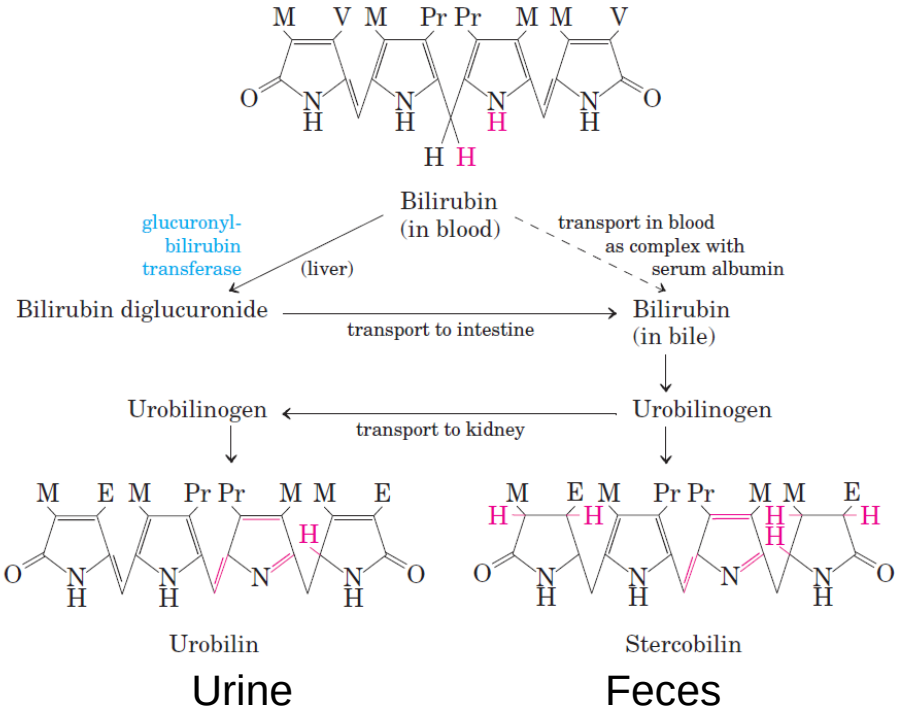
Structures are shown in linear form, rather than in their correct stereochemical conformations.



Fe^{2+} is quickly bound by ferritin.

Yellow

Green



In the liver, bilirubin is transformed to the bile pigment bilirubin diglucuronide. This product is sufficiently water-soluble to be secreted with other components of bile into the small intestine, where microbial enzymes convert it to several products, predominantly urobilinogen. Some urobilinogen is reabsorbed into the blood and transported to the kidney, where it is converted to urobilin, the compound that gives urine its yellow color. Urobilinogen remaining in the intestine is converted by microbes to stercobilin, which imparts the red-brown color to feces.

Impaired liver function or blocked bile secretion causes bilirubin to leak from the liver into the blood, resulting in a yellowing of the skin and eyeballs, a condition called **jaundice**. In cases of jaundice, determination of the concentration of bilirubin in the blood may be useful in the diagnosis of underlying liver disease.

Newborn infants sometimes develop jaundice because they have not yet produced enough glucuronyl bilirubin transferase to process their bilirubin. A traditional treatment to reduce excess bilirubin, exposure to a fluorescent lamp, causes a photochemical conversion of bilirubin to compounds that are more soluble and easily excreted.