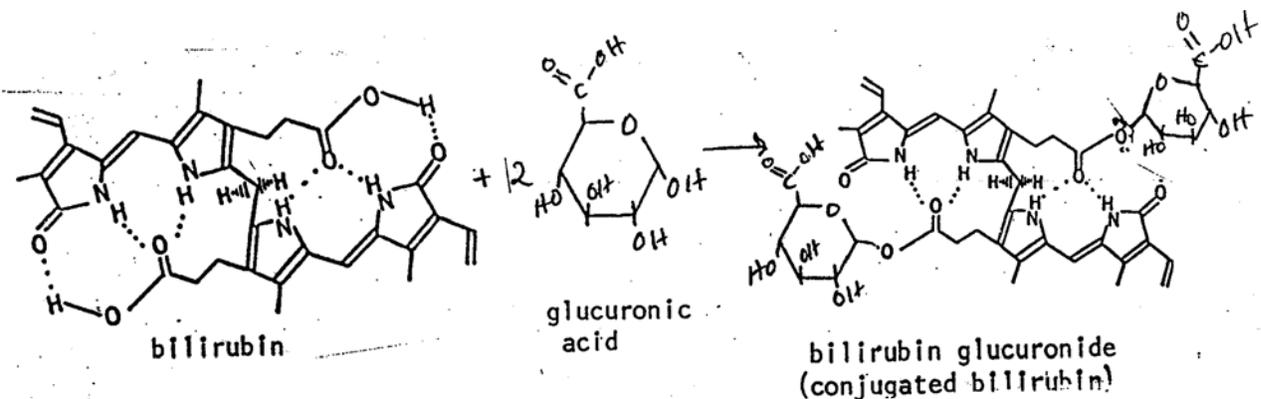


### 3.5 Photoisomerization Of Bilirubin

When red blood cells reach the end of their lifetime (about 3 months) they lyse and release red colored **hemoglobin**, the molecule that actually transports oxygen in the blood. The heme portion of hemoglobin is metabolized into orange colored **bilirubin**. A very small amount of bilirubin dissolves in urine and is responsible for the yellow color of urine, but the major route for excretion is more complex.

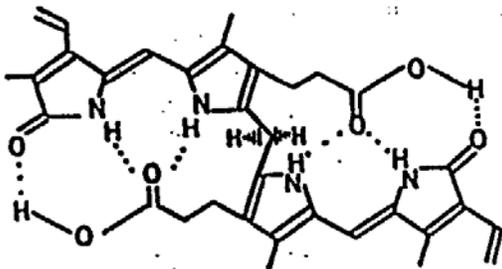
The major route for excretion of bilirubin is by excretion in bile into the small intestines and elimination in stools, but since stools are mostly water we have to make bilirubin more water soluble. The normal way of doing this is for the liver enzyme **glucuronyl transferase** to covalently attach two very polar molecules of **glucuronic acid (or glucuronate)** onto the nonpolar bilirubin molecule to make **bilirubin glucuronide**, commonly called **conjugated bilirubin**.



(What functional groups link the two glucuronic acid molecules to the bilirubin molecule? What functional groups in the original bilirubin and glucuronic acid molecules reacted to form that link?)

Conjugated bilirubin (bilirubin glucuronide) is much more water soluble and is excreted from the liver in bile and from there into the small intestine. In the large intestine bacteria metabolize it in a series of steps into **stercobilin** (from the Greek word *sterco* for poop), which has a brown color. However, if liver function is inadequate, there may be insufficient levels of the glucuronyl transferase enzyme to carry out the addition of glucuronic acid molecules to the bilirubin, and the bilirubin cannot be excreted in the stools;

There are some polar groups in the bilirubin molecule (OH, C=O, N-H) but the bilirubin folds up such that these polar groups are attracted to each other and internalized within a bilirubin molecule as shown below.



As a result, the surface of the bilirubin molecule is very nonpolar and bilirubin is not very soluble in water. Being nonpolar, high concentrations of bilirubin build up in the fatty tissues and membranes in the body. Since bilirubin is a yellow-orange colored compound, this produces **jaundice**.

There are three common situations in which liver function is impaired sufficiently to produce jaundice.

1. hepatitis
2. cirrhosis of the liver due to alcoholism
3. immature liver function in babies, especially common in premature babies resulting in **neonatal jaundice**

The third condition has serious long term consequences for the baby's mental growth because high levels of bilirubin in the brain can inhibit development of the baby's brain cells and cause permanent retardation. Consequently if blood bilirubin level gets too high (more than about 15 mg/dL for substantial lengths of time), measures are often taken to reduce blood bilirubin levels. This used to involve expensive blood transfusions, but it was noticed that babies with neonatal jaundice who were exposed to natural sunlight had increased urinary excretion rates of bilirubin. Further study showed that exposure to blue light causes the increased bilirubin excretion in the urine. Neonatal jaundice is treated with a **bili-light** that exposes the baby's skin to high intensity blue light. How does the bili-light work? Upon exposure to blue light, one of the C=C double bond adjacent to the 5-membered ring in bilirubin **photoisomerizes**.





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