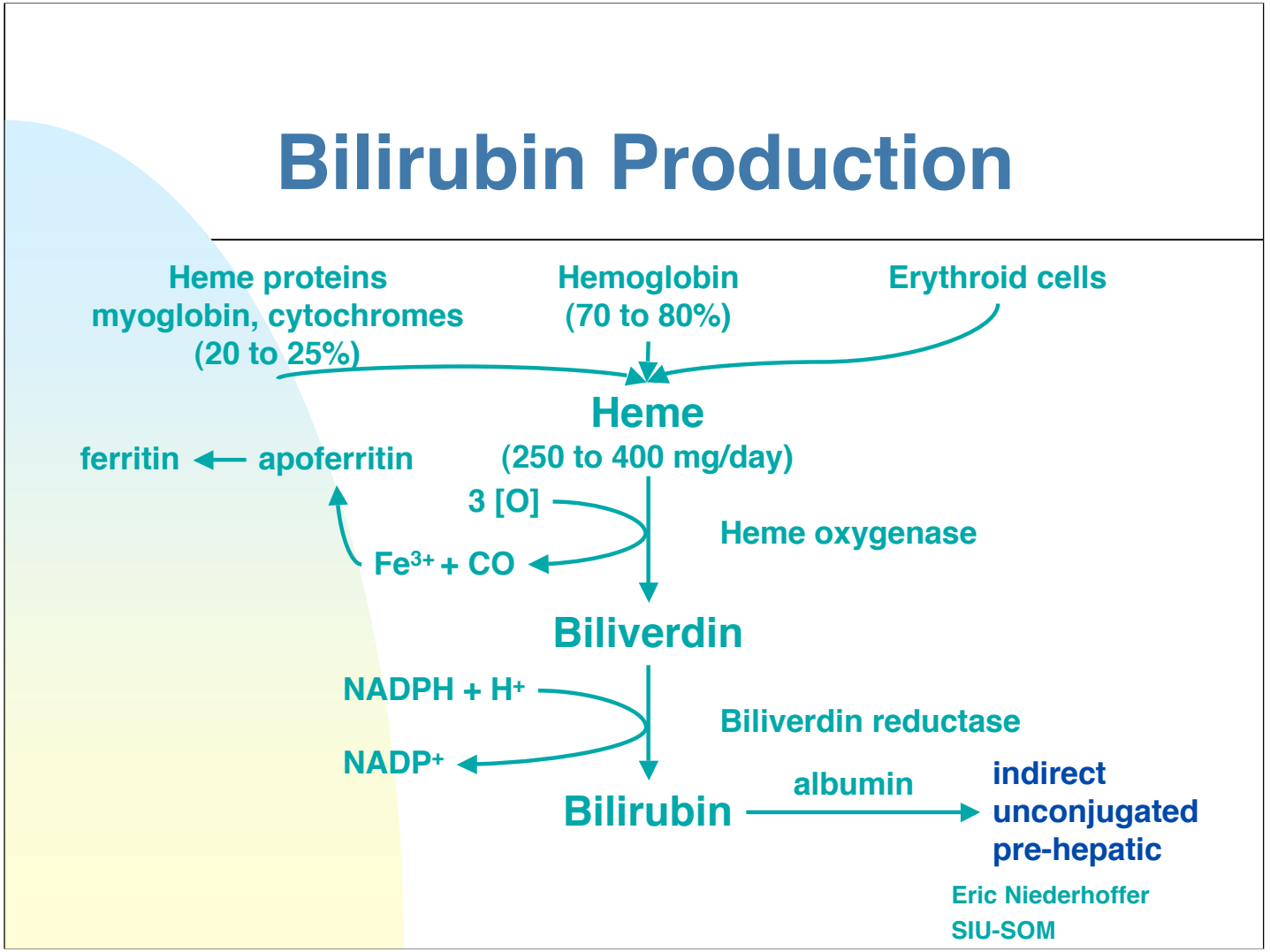
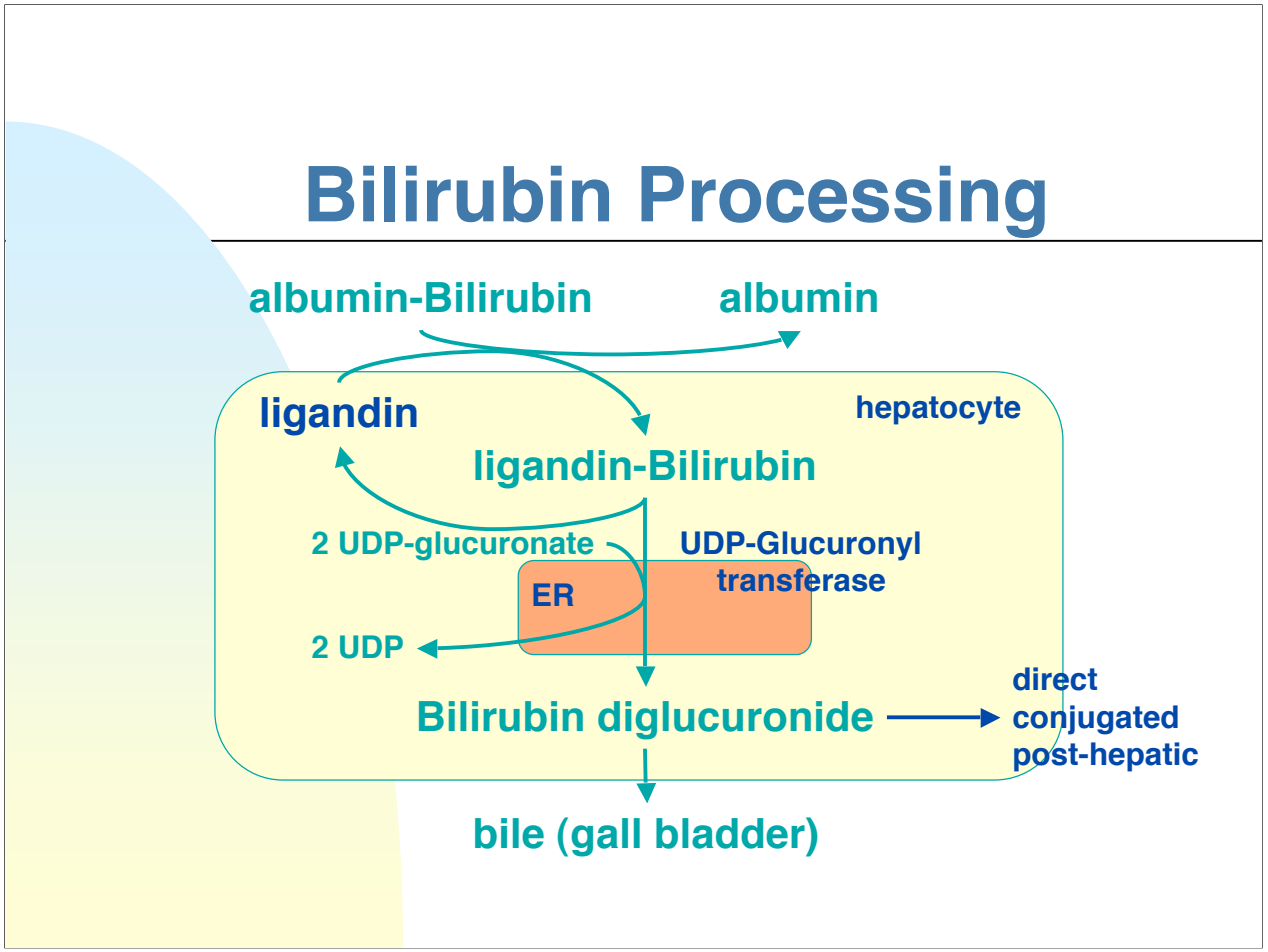


Heme is degraded by reticuloendothelial cells (mononuclear phagocytes of the spleen, liver, and bone marrow).

Bilirubin is insoluble in water and is responsible for the toxic effects. This unconjugated (indirect) bilirubin is transported in the serum bound to albumin.

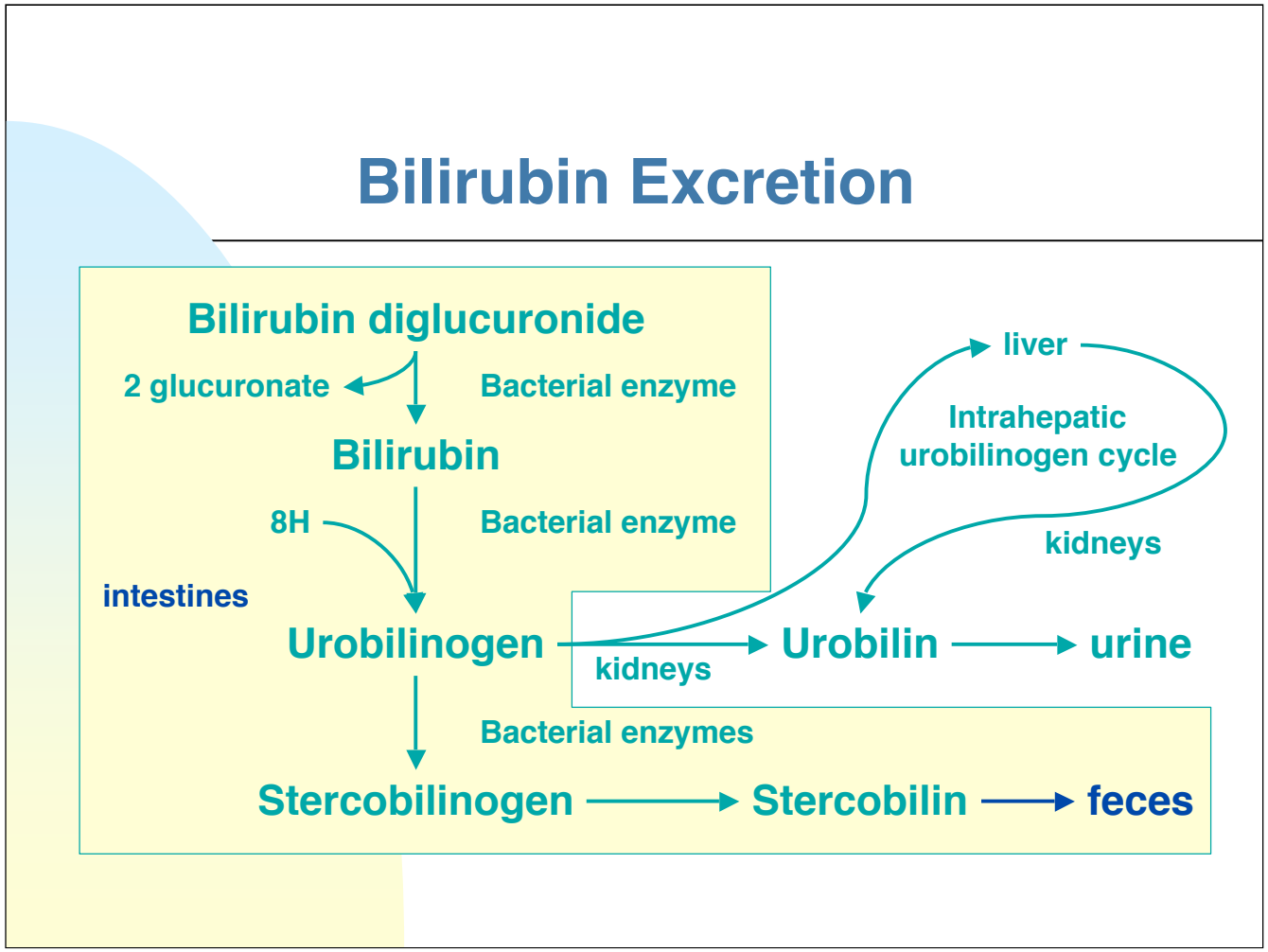


UDP: uridine diphosphate **ER**: endoplasmic reticulum

Unconjugated (indirect, pre-hepatic) bilirubin is transported from the surface of the hepatocyte to the endoplasmic reticulum through the binding of ligandin.

Glucuronic acid is added to bilirubin (catalyzed by glucuronyl transferase) to produce the conjugated (direct) mono- and diglucuronides. UDP-glucuronyl transferase deficiencies - mild deficiency (Glibert's syndrome), severe deficiency (Crigler-Najjar)

Conjugated bilirubins, which are water soluble, may be excreted in the urine and feces. The diglucuronide is primarily excreted in normal bile. Almost all of the bilirubin produced is excreted as one of the components of bile salts. Bilirubin is the pigment that gives bile its characteristic bright greenish yellow color.



When the bile salts reach the intestine via the common bile duct, the bilirubin is acted on by bacteria to form chemical compounds called urobilinogens. Most of the urobilinogen is excreted in the feces; some is reabsorbed and goes through the liver again and a small amount is excreted in the urine. Urobilinogen gives feces their dark color. An absence of bilirubin in the intestine, such as may occur with bile duct obstruction, blocks the conversion of bilirubin to urobilinogen, resulting in clay-colored stools.

Some of the urobilinogen that is produced in the intestine is reabsorbed and recycled through the liver.

Bilirubin Lab values

Bilirubin form	Normal value
Pre-hepatic, unconjugated, indirect	0.1 to 1.0 mg/dL
Post-hepatic, conjugated, direct	0.0 to 0.4 mg/dL
Fecal urobilinogen	40 to 280 mg/day

Conjugated bilirubin - water soluble - direct reaction with dyes

Unconjugated bilirubin - water insoluble - alcohol is needed for dye (indirect) reaction

Observe the color changes associated with heme degradation by watching the progress of a bruise (dark red to green to yellow).

Elevated serum bilirubin levels - increased production, decreased conjugation, decreased secretion by the liver, or blockage of the bile ducts. In cases of increased production, or decreased conjugation, the unconjugated or indirect form of bilirubin will be elevated.

Unconjugated hyperbilirubinemia - accelerated erythrocyte hemolysis in the newborn (erythroblastosis fetalis), absence of glucuronyl transferase, or hepatocellular disease.

Conjugated hyperbilirubinemia - obstruction of the biliary ducts, as with gallstones or hepatocellular diseases such as cirrhosis or hepatitis.

Elevated serum bilirubin test results may also be caused by the effects of many different drugs, including antibiotics, barbiturates, steroids, or oral contraceptives.

Chronic acquired liver diseases, the serum bilirubin concentration is usually normal until a significant amount of liver damage has occurred and cirrhosis is present.

Acute liver disease, the bilirubin is usually increased in relation to the severity of the acute process.

Review Questions

- How is bilirubin produced?
- How is bilirubin transported in the blood?
- How is bilirubin eliminated from the body?
- What is the intrahepatic urobilinogen cycle?
- What clinical observations would you make concerning a patient's inability to process bilirubin normally?