Bilirubin Metabolism Overview

Bilirubin is a yellowish pigment found in several tissues including the blood, liver, and gastrointestinal tract. In the blood, degenerating red blood cells release heme, which is metabolized by macrophages into unconjugated bilirubin. Unconjugated bilirubin travels in the blood bound to albumin until it reaches the liver. In the liver, it undergoes conjugation by UDP-glucuronosyltransferase. This conjugated bilirubin is water-soluble, so it is secreted into the bile (major) and blood (minor). When bile is secreted into the duodenal lumen, conjugated bilirubin follows it until it reaches the colon where bacteria convert it to urobilinogen. Urobilinogen either continues its journey through the colon until it is eliminated in the feces or is reabsorbed into the blood. If reabsorbed, it can travel to the kidneys to be eliminated in the urine or it can find its way back to the liver where it can be converted back into conjugated bilirubin and re-enter the bile. This is called enterohepatic circulation of bilirubin.



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Blood

Unconjugated Bilirubin

Broken-congos Belly-ribbon-dancer

Unconjugated bilirubin (indirect bilirubin) is a product of heme breakdown. Unconjugated bilirubin is insoluble and travels in the blood attached to albumin. Conditions that result in increased heme breakdown (e.g., hemolysis, infections) can lead to increased levels of unconjugated bilirubin.

Bound to Albumin

Album-man

Unconjugated bilirubin is insoluble (hydrophobic). It is carried through the circulation bound to albumin through a non-covalent bond. Unbound unconjugated bilirubin is neurotoxic.

Heme

Heme-man

Heme is a component of hemoglobin. It is a metal complex containing iron that can bind and release oxygen. Degradation of heme by heme oxygenase results in the formation of biliverdin, which is then reduced to unconjugated bilirubin by biliverdin reductase.

Red Blood Cells

Red Blood Cell

Red blood cells contain a protein called hemoglobin, which gives them a red color and plays a crucial role in the exchange of oxygen and carbon dioxide, primarily acting as a carrier of these molecules. Degradation of hemoglobin results in the formation of bilirubin.

Macrophages

Mac-man

Damaged red blood cells are recognized and degraded by macrophages of the liver and spleen, which degrade heme into unconjugated bilirubin.

Liver

Conjugated Bilirubin

Congo Belly-ribbon-dancer

Conjugation of unconjugated bilirubin with glucuronate results in the formation of conjugated bilirubin, which is water-soluble and can be excreted in the bile. Conjugated bilirubin is then metabolized by the gut bacteria into urobilinogen, which is excreted in the feces as stercobilin and gives the stool a brown color. Conditions that result in obstruction of bile flow (e.g., stones, tumors, or strictures in the biliary system) result in increased levels of conjugated bilirubin.

Secreted into Bile

Bile

After bilirubin is conjugated, the conjugated form is actively secreted into the bile canaliculi and reaches the small intestine. A minority of the conjugated bilirubin also enters the interstitial space and bloodstream. When there is an obstruction of bile flow, conjugated bilirubin backs up in the blood, and the

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levels rise above the normal values (<0.3 mg/dL).

Bowel

Urobilinogen

Euro-belly-genie

Urobilinogen is synthesized by the bacteria in the intestines. A minor portion of urobilinogen is reabsorbed into the blood and reaches the liver and kidneys. The reduction of urobilinogen results in the formation of urobilin, which gives the urine its yellowish color. The proportion of urobilinogen that doesn't get reabsorbed is directly reduced to stercobilin, a brown pigment that gives the fecal matter its brown color.

Eliminated in Feces

Eliminating Feces

A portion of urobilinogen is fecally eliminated and reduced to a brown pigment known as stercobilin. This process takes place in the intestine by the action of intestinal bacteria.

Eliminated in Urine

Eliminating Urine

The proportion of urobilinogen that is reabsorbed in the blood also ends up in the urine, where the reduction of urobilinogen results in the formation of urobilin, a yellow pigment that gives the urine its yellowish color.

Enterohepatic Circulation

Intestines-liver Circulating-arrows

Circulation of bilirubin, biliary acids, and other substances (eg, drugs) between the liver and intestines is known as enterohepatic circulation. This process involves the transport of substances from the liver to the small intestine through bile, absorption of these substances into the blood through enterocytes, and retrograde transport to the liver.

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