**Normal heme metabolism**

**Prehepatic metabolism**

* When red blood cells complete their lifespan of about 120 days, or if they are damaged, they rupture as they pass through the [reticuloendothelial system](https://en.wikipedia.org/wiki/Reticuloendothelial_system" \o "Reticuloendothelial system) (the spleen), and cell contents including [hemoglobin](https://en.wikipedia.org/wiki/Hemoglobin) are released into circulation. Macrophages phagocytose free hemoglobin and split it into [heme](https://en.wikipedia.org/wiki/Heme" \o "Heme) and [globin](https://en.wikipedia.org/wiki/Globin). Two reactions then take place with the heme molecule. The first [oxidation](https://en.wikipedia.org/wiki/Oxidation) reaction is catalyzed by the microsomal enzyme [heme oxygenase](https://en.wikipedia.org/wiki/Heme_oxygenase" \o "Heme oxygenase) and results in [biliverdin](https://en.wikipedia.org/wiki/Biliverdin" \o "Biliverdin) (green color pigment), [iron](https://en.wikipedia.org/wiki/Iron), and [carbon monoxide](https://en.wikipedia.org/wiki/Carbon_monoxide). The next step is the reduction of biliverdin to a yellow color  pigment called bilirubin . This bilirubin is "**unconjugated**", "**free**", or "**indirect**" bilirubin which is **lipid soluble**. Around 4 mg of bilirubin per kg of blood are produced each day. The majority of this bilirubin comes from the breakdown of heme from expired red blood cells .
* **Hepatic metabolism**

Once unconjugated bilirubin arrives in the liver, the unconjugated bilirubin is linked to  [glucuronic acid](https://en.wikipedia.org/wiki/Glucuronic_acid) producing  (conjugated bilirubin). Bilirubin that has been conjugated by the liver is **water-soluble** and excreted into the bile ducts.

**Posthepatic metabolism**

* Bilirubin enters the intestinal tract via bile. In the intestinal tract, bilirubin is converted into [urobilinogen](https://en.wikipedia.org/wiki/Urobilinogen" \o "Urobilinogen) by symbiotic intestinal bacteria. Most urobilinogen is converted into [stercobilinogen](https://en.wikipedia.org/wiki/Stercobilinogen" \o "Stercobilinogen) and further oxidized into [stercobilin](https://en.wikipedia.org/wiki/Stercobilin" \o "Stercobilin). Stercobilin is excreted via [feces](https://en.wikipedia.org/wiki/Feces), giving stool its characteristic brown coloration.

**Jaundice**

* Jaundice comes from the French jaune, meaning yellow, jaunisse meaning "yellow disease".
* Jaundice is a yellowish or greenish pigmentation of the skin and whites of the eyes due to high bilirubin levels. Jaundice in adults is typically a sign indicating the presence of underlying diseases involving abnormal heme metabolism, liver dysfunction, or biliary-tract obstruction.
* The prevalence of jaundice in adults is rare, it is common in babies in the first months of life due to immature liver.
* Normal levels of bilirubin in blood are below 1.0 mg/dl (17 μmol/L),
* jaundice become clear when levels of serum bilirubin is over 3 mg/dl (51 μmol/L) .

**Causes**

Jaundice is classified into three categories, depending on which part of the physiological mechanism involved. The three categories are:

**Prehepatic causes**

Prehepatic jaundice is most commonly caused by a pathological increased rate of red blood cell (erythrocyte) [hemolysis](https://en.wikipedia.org/wiki/Hemolysis). The increased breakdown of erythrocytes → increased unconjugated serum bilirubin → increased deposition of unconjugated bilirubin into the tissues. These diseases may cause jaundice due to increased erythrocyte hemolysis:

* [Sickle-cell anemia](https://en.wikipedia.org/wiki/Sickle-cell_anemia).
* Congenital [Spherocytosis](https://en.wikipedia.org/wiki/Spherocytosis).
* [Thalassemia](https://en.wikipedia.org/wiki/Thalassemia).
* [Glucose-6-phosphate dehydrogenase deficiency](https://en.wikipedia.org/wiki/Glucose-6-phosphate_dehydrogenase_deficiency) (favism).
* Malaria.

**Hepatic causes**

Hepatic jaundice is caused by abnormal liver metabolism of bilirubin. The major causes of hepatic jaundice are significant damage to hepatocytes due to infectious, drug/medication-induced, autoimmune etiology, or less commonly, due to inheritable genetic diseases. The following is a list of hepatic causes to jaundice:

* [Acute viral hepatitis](https://en.wikipedia.org/wiki/Acute_hepatitis) like A, B, C.
* [Chronic hepatitis](https://en.wikipedia.org/wiki/Chronic_hepatitis).
* [Cirrhosis](https://en.wikipedia.org/wiki/Cirrhosis).
* [Alcoholic liver disease](https://en.wikipedia.org/wiki/Alcoholic_liver_disease).

**Post-hepatic causes (Obstructive jaundice)**

Posthepatic jaundice (obstructive jaundice), is caused by a blockage of bile ducts that transport bile containing conjugated bilirubin out of the liver for excretion. This is a list of conditions that can cause posthepatic jaundice:

* Bile duct gallstones, It is the most common cause of obstructive jaundice.
* [Pancreatic cancer](https://en.wikipedia.org/wiki/Pancreatic_cancer) of the pancreatic head.
* [Cholestasis of pregnancy](https://en.wikipedia.org/wiki/Cholestasis_of_pregnancy)
* [Pancreatitis](https://en.wikipedia.org/wiki/Acute_pancreatitis)

Diagnosis,

* **urinalysis** to [measure the amount](https://www.healthline.com/health/urinalysis) of certain substances in urine
* **blood tests**, such as a [complete blood count (CBC)](https://www.healthline.com/health/cbc) or [liver function tests](https://www.healthline.com/health/liver-function-tests) to measure bilirubin and other substances in the blood
* **imaging tests**, such as [ultrasound](https://www.healthline.com/health/ultrasound) or MRI , to examine liver, gallbladder, and bile ducts to look for any obstruction
* **Endoscopy** for diagnosis and treatment like clipping varicose vein.
* **ERCP** :- endoscopic retrograde pancreaticography.
* **MRCP,** magnetic resonance cholengio-pancriatico-graphy.

Treatmant

* 1. pre hepatic:- treat infection like malaria, splenctomy. it may involve blood transfusion.
  2. Hepatic:- Treat hepatitis , stop liver damage through avoidance of toxic precipitants like drugs.
  3. Post hepatic:- surgery to release any obstruction to the bile duct, stopping any medication that damage the liver.

Manifestations and Complications

1. Anemia can occur in cases of RBC destruction.
2. When un conjugated Bilirubin levels increased it deposited in the brain tissue that can leads to brain damage.
3. Deposition in skin can lead to pruritis especially unconjugated type.
4. In many cases of RBC destruction in spleen it can leads to splenomegaly.
5. Liver cirrhosis can leads to portal hypertension and subsequent Esophageal or gastric Varicose Vein that can bleed and could be fatal.
6. Pale stool and dark urine.