**Jaundice**,

## terminology

Jaundice comes from the French  jaune, meaning yellow, jaunisse meaning "yellow disease". The medical term for it is icterus from the Greek word ikteros. The origin of the word icterus is coming from an ancient belief that jaundice could be cured from looking at the yellow bird icteria. The term icterus is sometimes incorrectly used to refer to jaundice specifically of sclera

 also known as **icterus**, is a yellowish or greenish pigmentation of the [skin](https://en.wikipedia.org/wiki/Skin) and [whites of the eyes](https://en.wikipedia.org/wiki/Sclera) due to [high bilirubin levels](https://en.wikipedia.org/wiki/Hyperbilirubinemia). Jaundice in adults is typically a sign indicating the presence of underlying diseases involving abnormal [heme](https://en.wikipedia.org/wiki/Heme%22%20%5Co%20%22Heme) [metabolism](https://en.wikipedia.org/wiki/Heme_oxygenase), [liver dysfunction](https://en.wikipedia.org/wiki/Liver_dysfunction), or [biliary-tract](https://en.wikipedia.org/wiki/Biliary_tract) obstruction. The prevalence of jaundice in adults is rare, while [jaundice in babies](https://en.wikipedia.org/wiki/Neonatal_jaundice) is common, with an estimated 80% affected during their first weeks of life. The most commonly associated symptoms of jaundice are [itchiness](https://en.wikipedia.org/wiki/Biliary_pruritus), pale [feces](https://en.wikipedia.org/wiki/Feces), and [dark urine](https://en.wikipedia.org/wiki/Dark_urine).

Normal levels of bilirubin in [blood](https://en.wikipedia.org/wiki/Blood_plasma) are below 1.0 [mg](https://en.wikipedia.org/wiki/Milligram)/[dl](https://en.wikipedia.org/wiki/Decilitre) (17 [μmol](https://en.wikipedia.org/wiki/Mole_%28unit%29%22%20%5Co%20%22Mole%20%28unit%29)/[L](https://en.wikipedia.org/wiki/Litre)), while levels over 2–3 mg/dl (34-51 μmol/L) typically result in jaundice. [High blood bilirubin](https://en.wikipedia.org/wiki/Hyperbilirubinemia) is divided into two types - unconjugated and conjugated bilirubin.

### 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%22%20%5Co%20%22Reticuloendothelial%20system) (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%22%20%5Co%20%22Heme) 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%22%20%5Co%20%22Heme%20oxygenase) and results in [biliverdin](https://en.wikipedia.org/wiki/Biliverdin%22%20%5Co%20%22Biliverdin) (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 [tetrapyrrole](https://en.wikipedia.org/wiki/Tetrapyrrole%22%20%5Co%20%22Tetrapyrrole) pigment called bilirubin by cytosolic enzyme [biliverdin reductase](https://en.wikipedia.org/wiki/Biliverdin_reductase%22%20%5Co%20%22Biliverdin%20reductase). This bilirubin is "unconjugated", "free", or "indirect" bilirubin. 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 in the process just described.

#### Hepatic metabolism

Once unconjugated bilirubin arrives in the liver, liver enzyme [UDP-glucuronyl transferase](https://en.wikipedia.org/wiki/UDP-glucuronyl-transferase) conjugates bilirubin + [glucuronic acid](https://en.wikipedia.org/wiki/Glucuronic_acid%22%20%5Co%20%22Glucuronic%20acid) → [bilirubin diglucuronide](https://en.wikipedia.org/wiki/Bilirubin_diglucuronide) (conjugated bilirubin). Bilirubin that has been conjugated by the liver is water-soluble and excreted into the gallbladder.

#### Posthepatic metabolism

Bilirubin enters the intestinal tract via bile. In the intestinal tract, bilirubin is converted into [urobilinogen](https://en.wikipedia.org/wiki/Urobilinogen%22%20%5Co%20%22Urobilinogen) by symbiotic intestinal bacteria. Most urobilinogen is converted into [stercobilinogen](https://en.wikipedia.org/wiki/Stercobilinogen%22%20%5Co%20%22Stercobilinogen) and further oxidized into [stercobilin](https://en.wikipedia.org/wiki/Stercobilin%22%20%5Co%20%22Stercobilin). Stercobilin is excreted via [feces](https://en.wikipedia.org/wiki/Feces), giving stool its characteristic brown coloration. A small portion of urobilinogen is reabsorbed back into the gastrointestinal cells. Most reabsorbed urobilinogen undergoes hepatobiliary recirculation. A smaller portion of reabsorbed urobilinogen is filtered into the kidneys. In the urine, urobilinogen is converted to [urobilin](https://en.wikipedia.org/wiki/Urobilin%22%20%5Co%20%22Urobilin), which gives urine its characteristic yellow color.

Other conditions can also cause yellowish skin, but are not jaundice, including [carotenemia](https://en.wikipedia.org/wiki/Carotenemia%22%20%5Co%20%22Carotenemia), which can develop from eating large amounts of foods containing [carotene](https://en.wikipedia.org/wiki/Carotene) — or medications such as [rifampin](https://en.wikipedia.org/wiki/Rifampin).

**Sign and symptom**

The most common signs of jaundice in adults are a yellowish discoloration of the white area of the eye ([sclera](https://en.wikipedia.org/wiki/Sclera)) and skin with scleral icterus presence indicating a serum bilirubin of at least 3 mg/dl. Other common signs include dark urine ([bilirubinuria](https://en.wikipedia.org/wiki/Bilirubinuria%22%20%5Co%20%22Bilirubinuria)) and pale ([acholia](https://en.wikipedia.org/wiki/Acholia%22%20%5Co%20%22Acholia)) fatty stool ([steatorrhea](https://en.wikipedia.org/wiki/Steatorrhea%22%20%5Co%20%22Steatorrhea)). Because bilirubin is a skin irritant, jaundice is commonly associated with severe itchiness.

Eye [conjunctiva](https://en.wikipedia.org/wiki/Conjunctiva) has a particularly high affinity for bilirubin deposition due to high elastin content. Slight increases in serum bilirubin can, therefore, be detected early on by observing the yellowing of sclerae. Disorders associated with a rise in serum levels of conjugated bilirubin during early development can also cause [dental hypoplasia](https://en.wikipedia.org/wiki/Enamel_hypoplasia)

**Causes**

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

|  |  |
| --- | --- |
| **Category** | hide**Definition** |
| Prehepatic/hemolytic | The pathology occurs prior to the liver metabolism, due to red blood cell rupture  |
| Hepatic/hepatocellular | The pathology is due to damage of parenchymal liver cells. |
| Posthepatic/cholestatic | The pathology occurs after bilirubin conjugation in the liver, due to obstruction of the biliary tract and/or decreased bilirubin excretion.[[21]](https://en.wikipedia.org/wiki/Jaundice#cite_note-21) |

**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 mucosal tissue. These diseases may cause jaundice due to increased erythrocyte hemolysis:

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

**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 hepatitis](https://en.wikipedia.org/wiki/Acute_hepatitis)
* [Chronic hepatitis](https://en.wikipedia.org/wiki/Chronic_hepatitis)
* [Hepatotoxicity](https://en.wikipedia.org/wiki/Hepatotoxicity)
* [Cirrhosis](https://en.wikipedia.org/wiki/Cirrhosis)
* [Drug-induced hepatitis](https://en.wikipedia.org/wiki/Drug-induced_hepatitis)
* [Alcoholic liver disease](https://en.wikipedia.org/wiki/Alcoholic_liver_disease)

**Posthepatic 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:

* [Choledocholithiasis](https://en.wikipedia.org/wiki/Common_bile_duct_stone) (common 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)

To diagnose pre-hepatic jaundice, likely order the following tests:

* **a 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 an MRI or [ultrasound](https://www.healthline.com/health/ultrasound), to examine liver, gallbladder, and bile ducts to rule out other forms of jaundice

**Treatments**

**For malaria:**

* medications to help destroy the parasite and prevent parasites from reinfecting liver again

**For sickle cell anemia:**

* blood transfusions from a healthy donor
* rehydrating with intravenous (IV) fluid
* medications for any infections that can cause a sickle cell crisis

**For spherocytosis:**

* folic acid supplements
* blood transfusions for anemia
* spleen removal surgery to help increase red blood cell life and lower the chance of [gallstones](https://www.healthline.com/health/gallstones)

**For thalassemia:**

* blood transfusions
* bone marrow transplants
* spleen or gallbladder removal surgery

#### Hepatic jaundice: pathophysiology

Hepatic jaundice (hepatocellular jaundice) is due to significant damage to liver function → hepatic cell death and necrosis occur → impaired bilirubin transport across hepatocytes. Bilirubin transport across [hepatocytes](https://en.wikipedia.org/wiki/Hepatocyte) may be impaired at any point between hepatocellular uptake of unconjugated bilirubin and hepatocellular transport of conjugated bilirubin into the gallbladder. In addition, subsequent cellular [edema](https://en.wikipedia.org/wiki/Oedema) due to inflammation causes mechanical obstruction of intrahepatic biliary tract. Most commonly, interferences in all three major steps of bilirubin metabolism — uptake, conjugation, and excretion — usually occur in hepatocellular jaundice. Thus, an abnormal rise in both unconjugated and conjugated bilirubin will be present. Because excretion (the rate-limiting step) is usually impaired to the greatest extent, conjugated hyperbilirubinemia predominates.

The unconjugated bilirubin still enters the liver cells and becomes conjugated in the usual way. This conjugated bilirubin is then returned to the blood, probably by rupture of the congested bile canaliculi and direct emptying of the bile into the [lymph](https://en.wikipedia.org/wiki/Lymph) leaving the liver. Thus, most of the bilirubin in the plasma becomes the conjugated type rather than the unconjugated type, and this conjugated bilirubin, which did not go to intestine to become urobilinogen, gives the urine the dark color.

Causes of hepatic jaundice are:

* [liver cirrhosis](https://www.healthline.com/health/cirrhosis), which means that liver tissues are scarred by long-term exposure to infections or toxic substances, such as high levels of alcohol
* [viral hepatitis](https://www.healthline.com/health/hepatitis), an inflammation of the liver caused by one of several viruses that can get into body through infected food, water, blood, stool, or sexual contact
* [primary biliary cirrhosis](https://www.healthline.com/health/primary-biliary-cirrhosis), which happens when bile ducts are damaged and can’t process bile, causing it to build up in the liver and damage liver tissue
* [alcoholic hepatitis](https://www.healthline.com/health/alcoholic-hepatitis), in which liver tissues are scarred by the heavy, long-term drinking of alcohol
* [liver cancer](https://www.healthline.com/health/liver-cancer), in which cancerous cells develop and multiply within liver tissues

Common symptoms of hepatic jaundice include:

* loss of appetite
* bloody nose
* skin itching
* weakness
* abnormal weight loss
* swelling of abdomen or legs
* dark urine or pale stool
* pain in muscles or joints
* darkening skin
* fever
* feeling sick
* throwing up

To diagnose hepatic jaundice, doctor will likely order the following tests:

* **a urinalysis** to measure levels of substances in urine related to liver function
* **blood tests**, such as a [complete blood count (CBC)](https://www.healthline.com/health/cbc) and antibody tests, or [liver function tests](https://www.healthline.com/health/liver-function-tests) to measure bilirubin in the blood and levels of substances that indicate that liver may not be processing bilirubin properly
* **imaging tests**, such as an MRI or [ultrasound](https://www.healthline.com/health/ultrasound), to examine liver for damage or for the presence of cancerous cells
* **an endoscopy**, [which involves](https://www.healthline.com/health/endoscopy) inserting a thin, lighted tube into a small incision to look at liver and take a tissue sample (biopsy) if necessary for analysis for cancer or other conditions

Treatment for hepatic jaundice can include:

**For liver cirrhosis:**

* quitting drinking
* beta-blockers
* intravenous (IV) antibiotics
* a [low-protein diet](https://www.healthline.com/nutrition/low-protein-diet)

**For viral hepatitis:**

* antiviral medications
* hepatitis vaccination
* plenty of rest and fluids

**For primary biliary cirrhosis:**

* bile acids to help with digestion
* bile-lowering medication
* antihistamines like diphenhydramine (Benadryl) for itching

**For alcoholic hepatitis:**

* quitting alcohol
* nutrition supplements
* liver transplant, in severe cases

**For liver cancer:**

* chemotherapy or radiation to kill cancer cells
* partial liver resection
* liver transplant

#### Posthepatic pathophysiology

Posthepatic jaundice (obstructive jaundice) is due to a blockage of bile excretion from the biliary tract → increased conjugated bilirubin and bile salts. In complete obstruction of the bile duct, conjugated bilirubin cannot access the intestinal tract → no further bilirubin conversion to urobilinogen → no stercobilin or urobilin. Instead, excess conjugated bilirubin is filtered into the urine without urobilinogen in obstructive jaundice. Conjugated bilirubin in urine (bilirubinuria) gives urine an abnormally dark brown color. Thus, the presence of pale stool (stercobilin absent from feces) and dark urine (conjugated bilirubin present in urine) suggest an obstructive cause of jaundice. Because these associated signs are also positive in many hepatic jaundice conditions, they cannot be a reliable clinical feature to distinguish obstruction versus hepatocellular jaundice causes.

The [most common causes](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1119305/) of post-hepatic jaundice are:

* [gallstones](https://www.healthline.com/health/gallstones), hard calcium deposits in the gallbladder that can block bile ducts
* [pancreatic cancer](https://www.healthline.com/health/pancreatic-cancer), the development and spread of cancer cells in the [pancreas](https://www.healthline.com/human-body-maps/pancreas), an organ that helps produce digestive substances
* [bile duct cancer](https://www.healthline.com/health/bile-duct-cancer), the development and spread of cancer cells in bile ducts
* [pancreatitis](https://www.healthline.com/health/pancreatitis), an inflammation or infection of pancreas

Common symptoms of post-hepatic jaundice include:

* feeling sick
* throwing up
* dark urine or pale stool
* abdominal pain
* diarrhea
* abnormal weight loss
* skin itching
* abdominal swelling
* fever

Some risk factors for this type of jaundice include:

* being overweight
* eating a high-fat, low-fiber diet
* having [diabetes mellitus](https://www.healthline.com/health/diabetes)
* having a family history of gallstones
* being female
* aging
* smoking tobacco products
* drinking a lot of alcohol
* having a previous pancreas inflammation or infection
* being exposed to industrial chemicals

To diagnose post-hepatic jaundice, doctor will likely order the following tests:

* **a urinalysis** to measure levels of substances in urine
* **blood tests**, such as a [complete blood count (CBC)](https://www.healthline.com/health/cbc) and antibody tests for cancer, or [liver function tests](https://www.healthline.com/health/liver-function-tests) to rule out hepatic jaundice
* **imaging tests**, such as an MRI or [ultrasound](https://www.healthline.com/health/ultrasound), to examine liver, gallbladder, and bile ducts for obstructions like gallstones or tumors
* **an endoscopy**, which involves inserting a thin, lighted tube down the esophagus to look at liver, gallbladder, or bile ducts and take a tissue sample if necessary for analysis for cancer or other conditions

Treatment for post-hepatic jaundice will address the cause. This includes:

**For gallstones:**

* changing diet to stop producing gallstones
* removing gallstones or gallbladder entirely
* taking medications or treatments to dissolve gallstones

**For pancreatic cancer:**

* surgery to remove cancerous tissue or whole pancreas
* radiation or chemotherapy to destroy cancer cells

**For bile duct cancer:**

* surgery to remove bile ducts and parts of liver and pancreas
* radiation or chemotherapy to destroy cancer cells
* liver transplant

**For pancreatitis:**

* rest
* intravenous (IV) fluids or pain medication
* surgery to remove any causes of inflammation (like gallstones)

In the second reaction, [biliverdin](https://en.wikipedia.org/wiki/Biliverdin%22%20%5Co%20%22Biliverdin) is converted to [bilirubin](https://en.wikipedia.org/wiki/Bilirubin) by [biliverdin reductase](https://en.wikipedia.org/wiki/Biliverdin_reductase%22%20%5Co%20%22Biliverdin%20reductase) (BVR):

|  |  |  |
| --- | --- | --- |
| [biliverdin](https://en.wikipedia.org/wiki/Biliverdin) | [biliverdin reductase](https://en.wikipedia.org/wiki/Biliverdin_reductase) | [bilirubin](https://en.wikipedia.org/wiki/Bilirubin) |
| Biliverdin3.svg |   | Bilirubin ZZ.png |
|  |  |

Diagnosis

Most people presenting with jaundice have various predictable patterns of liver panel abnormalities, though significant variation does exist. The typical liver panel includes blood levels of enzymes found primarily from the liver, such as the [aminotransferases](https://en.wikipedia.org/wiki/Aminotransferases) (ALT, AST), and [alkaline phosphatase](https://en.wikipedia.org/wiki/Alkaline_phosphatase) (ALP); bilirubin (whiwqwwhch causes the jaundice); and protein levels, specifically, [total protein](https://en.wikipedia.org/wiki/Blood_proteins) and [albumin](https://en.wikipedia.org/wiki/Albumin). Other primary lab tests for liver function include [gamma glutamyl transpeptidase](https://en.wikipedia.org/wiki/Gamma_glutamyl_transpeptidase) (GGT) and [prothrombin time](https://en.wikipedia.org/wiki/Prothrombin_time%22%20%5Co%20%22Prothrombin%20time) (PT). No single test can differentiate between various classifications of jaundice. A combination of [liver function tests](https://en.wikipedia.org/wiki/Liver_function_tests) and other physical examination findings is essential to arrive at a diagnosis.

**Laboratory tests**.

|  |  |  |  |
| --- | --- | --- | --- |
|  | **Prehepatic jaundice** | **Hepatic jaundice** | **Posthepatic jaundice** |
| **Total serum bilirubin** | Normal / increased | Increased | Increased |
| **Conjugated bilirubin** | Normal | Increased | Increased |
| **Unconjugated bilirubin** | Normal / increased | Increased | Normal |
| **Urobilinogen** | Normal / increased | Decreased | Decreased / negative |
| **Urine color** | Normal[[33]](https://en.wikipedia.org/wiki/Jaundice#cite_note-33) | Dark (urobilinogen, conjugated bilirubin) | Dark (conjugated bilirubin) |
| **Stool color** | Brown | Slightly pale | Pale, white |
| **Alkaline phosphatase levels** | Normal | Increased | Highly increased |
| **Alanine transferase and aspartate transferase levels** | Highly increased | Increased |
| **Conjugated bilirubin in urine** | Not present | Present | Present |

Unconjugated bilirubin is hydrophobic, so cannot be excreted in urine. Thus, the finding of increased urobilinogen in the urine without the presence of bilirubin in the urine (due to its unconjugated state) suggests hemolytic jaundice as the underlying disease process. Urobilinogen will be greater than 2 units (i.e., hemolytic anemia causes increased heme metabolism

## Complications

Hyperbilirubinemia, more precisely hyperbilirubinemia due to the unconjugated fraction, may cause bilirubin to accumulate in the [grey matter](https://en.wikipedia.org/wiki/Grey_matter) of the [central nervous system](https://en.wikipedia.org/wiki/Central_nervous_system), potentially causing irreversible neurological damage, leading to a condition known as [kernicterus](https://en.wikipedia.org/wiki/Kernicterus).

### Neonatal jaundice

Jaundice in infants presents with yellowed skin and icteral sclerae. Neonatal jaundice spreads in a cephalocaudal pattern, affecting the face and neck before spreading down to the trunk and lower extremities in more severe cases. Other symptoms may include drowsiness, poor feeding, and in severe cases, unconjugated bilirubin can cross the blood-brain barrier and cause permanent neurological damage ([kernicterus](https://en.wikipedia.org/wiki/Kernicterus)).

#### Causes

The most common cause of jaundice in infants is [normal physiologic jaundice](https://en.wikipedia.org/wiki/Physiologic_jaundice).

#### Pathophysiology

Normal physiological neonatal jaundice is due to immaturity of liver enzymes involved in bilirubin metabolism, immature gut microbiota, and increased breakdown of fetal hemoglobin (HbF).

While most cases of newborn jaundice are not harmful, if bilirubin levels are very high, brain damage — kernicterus — may occur leading to significant disability

#### Treatment

Jaundice in newborns is usually transient and dissipates without medical intervention. In cases when serum bilirubin levels are greater than 4–21 mg/dl (68-360 μmol/l), infant may be treated with [phototherapy](https://en.wikipedia.org/wiki/Phototherapy) or [exchanged transfusion](https://en.wikipedia.org/wiki/Exchanged_transfusion) depending on the infant's age and prematurity status.