





JAUNDICE

BY

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JAUNDICE

Jaundice (also called icterus) is a condition characterized by a yellow discoloration of the skin, sclera (whites of the eyes), and mucous membranes. It is caused by deposition of bilirubin secondary to increased bilirubin levels in the circulation.







- It can be caused by other yellow substances such as **carotene** or **certain drugs**.
- Conjugated bilirubin causes more jaundice than unconjugated bilirubin because of its **easier absorption into tissues** and **higher water solubility**.

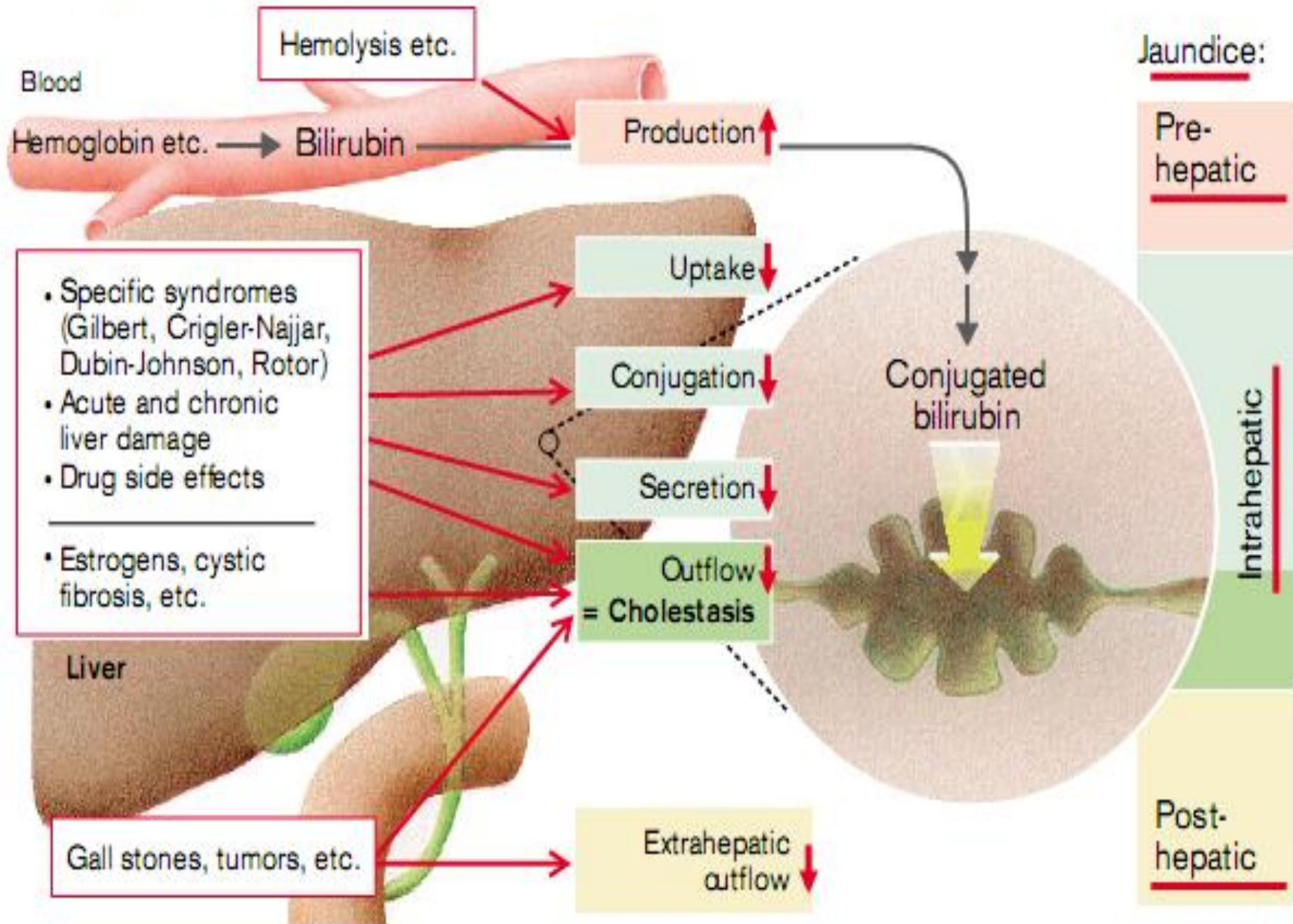
Types of jaundice

Jaundice can be classified into three major forms:

- A. Hemolytic jaundice (prehepatic).**
- B. Hepatocellular jaundice (Hepatic).**
- C. Obstructive jaundice (Posthepatic).**

In both **prehepatic** and **posthepatic** jaundice, the function of the liver itself is not impaired.

A. Types of Jaundice



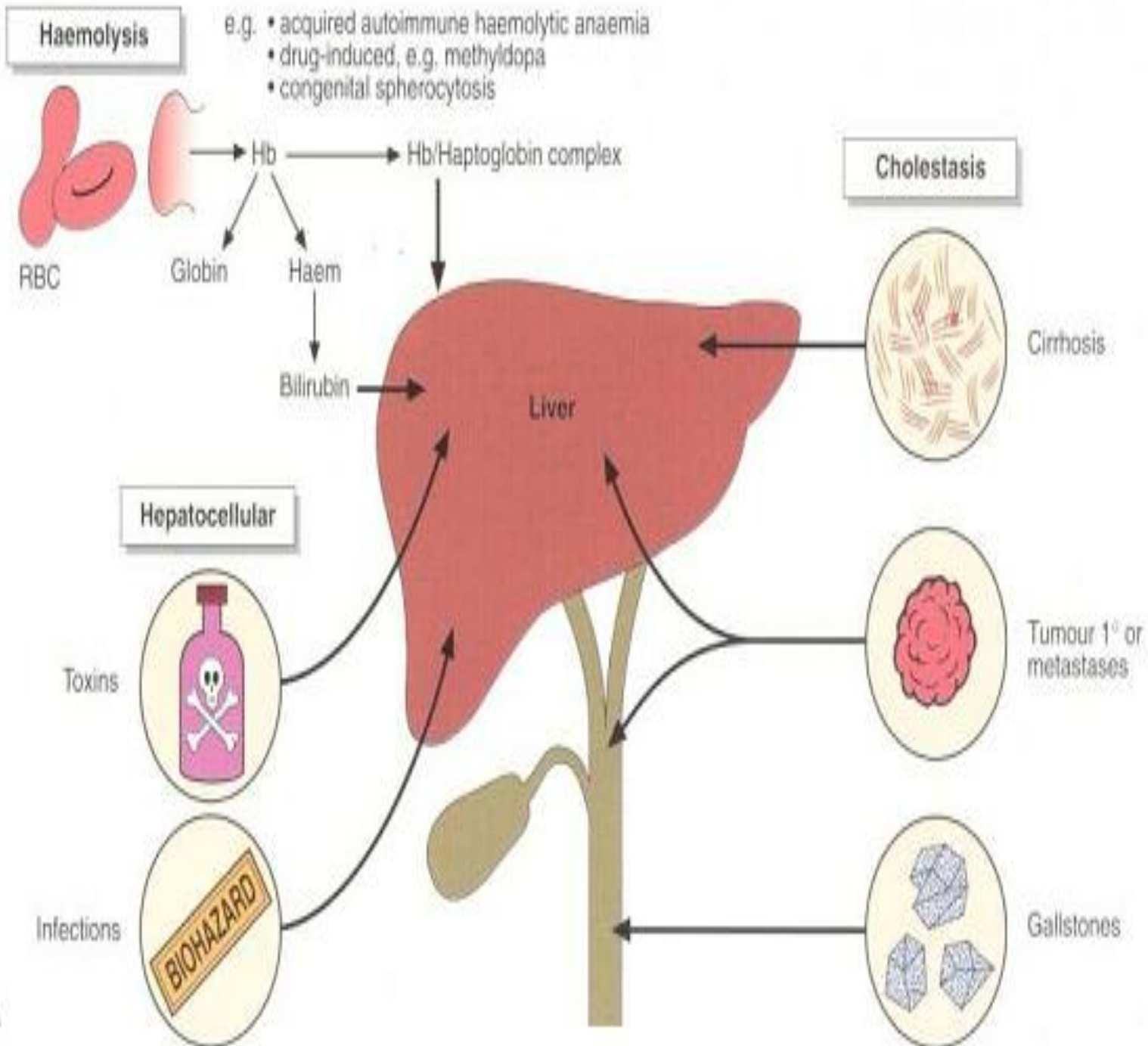


Fig. 3 Causes of jaundice.

a. Hemolytic jaundice (Prehepatic)

The liver has the capacity to **conjugate** and **excrete** over **3000 mg bilirubin per day**, whereas the normal production of bilirubin is only **300 mg/day**. This excess capacity allows the liver to respond to increased heme degradation with a corresponding increase in conjugation and secretion of bilirubin diglucuronide.

Prehepatic jaundice is caused by an increased production of bilirubin by the body.

There are four general causes:

1. Excessive destruction of circulating erythrocytes (hemolysis)
2. Ineffective erythropoiesis, resulting in an increased rate of destruction of immature and malformed red cells.
3. Increased turnover of nonhemoglobin heme compounds in the liver and other organs.
4. Phagocytic breakdown of extravasated red blood cells (hematoma).

- Increased hemolysis may be due to:
 - Hemolytic anemias.
 - Exposure to chemicals.
 - Hemolytic antigen-antibody reactions.
 - Disease states (some cancers).
 - Drugs coating red blood cells.
- **Ineffective erythropoiesis** is a pathologic process in which a very low proportion of red cells formed in the bone marrow enters the circulation and those remaining in the bone marrow are prematurely destroyed.

- Massive lysis of red blood cells (for example, in patients with sickle cell anemia or malaria) may produce bilirubin faster than the, liver can conjugate it.
- More bilirubin is excreted into the bile.
- The amount of urobilinogen entering the enterohepatic circulation is increased
- Urinary urobilinogen is increased.
- Unconjugated bilirubin is elevated in blood.

- In prehepatic jaundice, the production of bilirubin is below the capacity of the liver to conjugate and excrete it.
- In prehepatic jaundice no bilirubin found in the urine because the increase is in unconjugated bilirubin(not filtered through the glomerulus).

Causes of Prehepatic Jaundice



Hereditary Hemolytic Processes	<u>Hereditary spherocytosis</u> <u>G-6-PD deficiency</u> <u>Sickle cell disease</u> <u>Thalassemia</u> <u>Hemoglobin C disease</u>
Acquired Hemolytic Processes	<u>Hemolytic disease of the newborn</u> <u>Hemolytic transfusion reactions</u> <u>Drug-induced hemolytic anemia</u> <u>Autoimmune hemolytic anemia</u> <u>Paroxysmal nocturnal hemoglobinuria</u>
Ineffective <u>Erythropoiesis</u>	<u>Megaloblastic anemias</u> <u>Sideroblastic anemia</u> <u>Erythroleukemia</u> <u>Lead poisoning</u>
Physiologic jaundice of the Newborn	<u>Prematurity</u>
Impaired delivery of <u>bilirubin to the liver</u>	<u>Congestive heart failure</u>



b. Hepatocellular jaundice (Hepatic)

- Damage to liver cells (for example, in patients with cirrhosis or hepatitis) causes a decrease in both bilirubin uptake and production of conjugated bilirubin.

Hepatic Jaundice can be subdivided into two types:

A. Retention jaundice: defect in the transport of bilirubin into the hepatocyte.

B. Regurgitation jaundice: the hepatic cell is damaged or defective or the excretion of products from the hepatocyte is impaired.

- In retention jaundice, **unconjugated bilirubin** is the predominant type found in the plasma.
- In regurgitation jaundice, **conjugated bilirubin** is found in greater concentrations.
- Conjugation enzyme deficiencies, as in Gilbert's disease and Crigler-Najjar syndrome, **are examples of retention jaundice.**
- Dubin-Johnson syndrome, Rotor's syndrome, viral hepatitis, and toxic and neoplastic conditions **are examples of regurgitation jaundice.**

- Unconjugated bilirubin occurs in the blood.
- Increased urobilinogen in the urine.
- The urine is dark in color and stools are a pale, clay color.
- Plasma levels of AST (SCOT) and ALT (SGPT) are elevated and the patient experiences nausea and anorexia.

Causes of Hepatic jaundice



Retention Jaundice	Physiologic jaundice of the newborn Gilbert's syndrome <u>Crigler-Najjar syndrome, Types 1 and 11</u>
Regurgitation Jaundice	<u>Dubin-Johnson syndrome</u> Rotor's syndrome <u>Recurrent benign intrahepatic cholestasis</u> <u>Cholestatic jaundice of pregnancy</u> Cirrhosis Viral hepatitis Alcoholic liver disease Drug-induced liver disease Primary <u>biliary cirrhosis</u> Postoperative jaundice <u>Hepatocellular carcinoma</u> Toxic liver injury Autoimmune liver disease Inborn errors of metabolism

c. Obstructive jaundice (Posthepatic)

- Posthepatic jaundice, or obstructive jaundice, caused by a blockage of the flow of bile from the liver.
- Bile produced by the liver cannot be released into the intestines and overflows.
- Jaundice is not due to overproduction of bilirubin, but results from obstruction of the bile duct.

For example:

- The presence of a hepatic tumor or bile stones may block the bile ducts, preventing passage of bilirubin into the intestine.
- Patients with obstructive jaundice experience GI pain, nausea, and produce stools that are a pale, clay color.
- The liver "regurgitates" conjugated bilirubin into the blood, which is excreted in the urine.

Cause:

The most common obstructions are:

- Stones within the common bile duct.
- Neoplasm of the pancreas or other organ.
- Strictures caused by congenital defects in the ducts or by trauma to the ducts during abdominal surgery.
- Note: Prolonged obstruction of the bile duct can lead to liver damage and a subsequent rise in unconjugated bilirubin.



Causes of Posthepatic Jaundice

Common bile duct stone

Cancer of the bile ducts, pancreas, ampulla of Vater

Bile duct stricture or stenosis

Sclerosing cholangitis

Choledochal cysts

Biliary atresia in infants



Posthepatic jaundice characterized by:

- ✓ Increase plasma conjugated bilirubin.
- ✓ The quantity of bilirubin reaching the intestines is decreased resulting in the characteristic **clay-colored feces**. due to the decreased formation of **urobilinogen** in the intestines and its decreased excretion.
- ✓ very little or no **urobilinogen** but large quantities of **bilirubin** in the urine.
- ✓ yellow-orange urine color reflects excretion of bilirubin.

Expected Laboratory Results In Prehepatic, Hepatic, and Posthepatic Jaundice Conditions

Liver Function Test	Prehepatic Jaundice	Acute Hepatocellular Jaundice	Chronic Hepatocellular Jaundice	Posthepatic Jaundice
Total bilirubin	Nor. to incr.	Increased	Increased	Increased
Conjugated bilirubin	Nor. to incr.	Increased	Increased	Increased
Unconjugated bilirubin	Increased	Increased	Increased	Increased
Urine urobilinogen	Increased	Increased	Increased	Decreased
Urine bilirubin	Normal	Increased	Increased	Increased
Albumin	Normal	Normal	Decreased	Normal
Globulin	Normal	Normal	Increased	Normal
Aminotransferases	Normal	Increased	Increased	N. to slight incr.
Alkaline phosphatase	Normal	N. to 3 ×ULN	N. to 3 ×ULN	Inc. to 10 × ULN
Lactate dehydrogenase	Inc. & hemo.	Increased	Increased	Normal
BSP dye test	Normal	Increased	Increased	Increased
Prothrombin time	Normal	Normal	Prolonged	Normal

ULN – upper limits of normal.

Table 32-3. Laboratory results in normal patients and patients with three different causes of jaundice.

Condition	Serum Bilirubin	Urine Urobilinogen	Urine Bilirubin	Fecal Urobilinogen
Normal	Direct: 0.1–0.4 mg/dL Indirect: 0.2–0.7 mg/dL	0–4 mg/24 h	Absent	40–280 mg/24 h
Hemolytic anemia	↑ Indirect	Increased	Absent	Increased
Hepatitis	↑ Direct and indirect	Decreased if micro-obstruction is present	Present if micro-obstruction occurs	Decreased
Obstructive jaundice ¹	↑ Direct	Absent	Present	Trace to absent

d-Neonatal jaundice

- Neonatal jaundice is a condition defined as the newborn having total serum bilirubin levels above 15 mg/dL in the few days after birth or bilirubin levels persisting above 10 mg/dL for more than 2 weeks.
- The newborn have higher bilirubin concentration than adult because of the hemolysis occurring during birth as well as the infant's immature liver.

- Newborn infants, particularly premature babies, often accumulate bilirubin because the activity of **hepatic bilirubin glucuronyl transferase is low at birth** and reaches adult levels in about two weeks.
- Elevated bilirubin, in excess of the binding capacity of albumin, can diffuse into the basal ganglia and cause **toxic encephalopathy**.

- **Cause:**

- Before birth the fetus depend on the mother's liver to perform the necessary functions.
- The enzymes necessary for metabolism and conjugation are not present in sufficient concentrations at birth and do not function efficiently for a few days afterward.
- These two conditions, as well as an increased rate of absorption of unconjugated bilirubin from the infant's intestinal tract, often cause bilirubin levels to rise to 10 mg/dL
- Medical treatment to assist the removal of excess bilirubin and to prevent the development of *kernicterus*.

- **Kernicterus** is the deposition of unconjugated bilirubin in the central nervous system that may cause severe neurologic damage.

Several pathologic conditions cause these symptoms to continue .

such as:

- ✓ Biliary atresia.
- ✓ ABO.
- ✓ Rh incompatibility.
- ✓ Septicemia.
- ✓ Neonatal hepatitis.
- ✓ Inherited metabolic liver diseases

Treatment:

- Administration of **Phenobarbital** to induce enzyme activity or **phototherapy with monochromatic blue light** to cause the oxidation of bilirubin to more soluble end products and enhance the renal excretion of the bilirubin.
- Thus, newborns with markedly elevated bilirubin levels are treated with **blue fluorescent light**, which converts bilirubin to more polar and, hence, water-soluble isomers. These photoisomers can be excreted into the bile without conjugation to glucuronic acid.

Neonatal jaundice light treatment



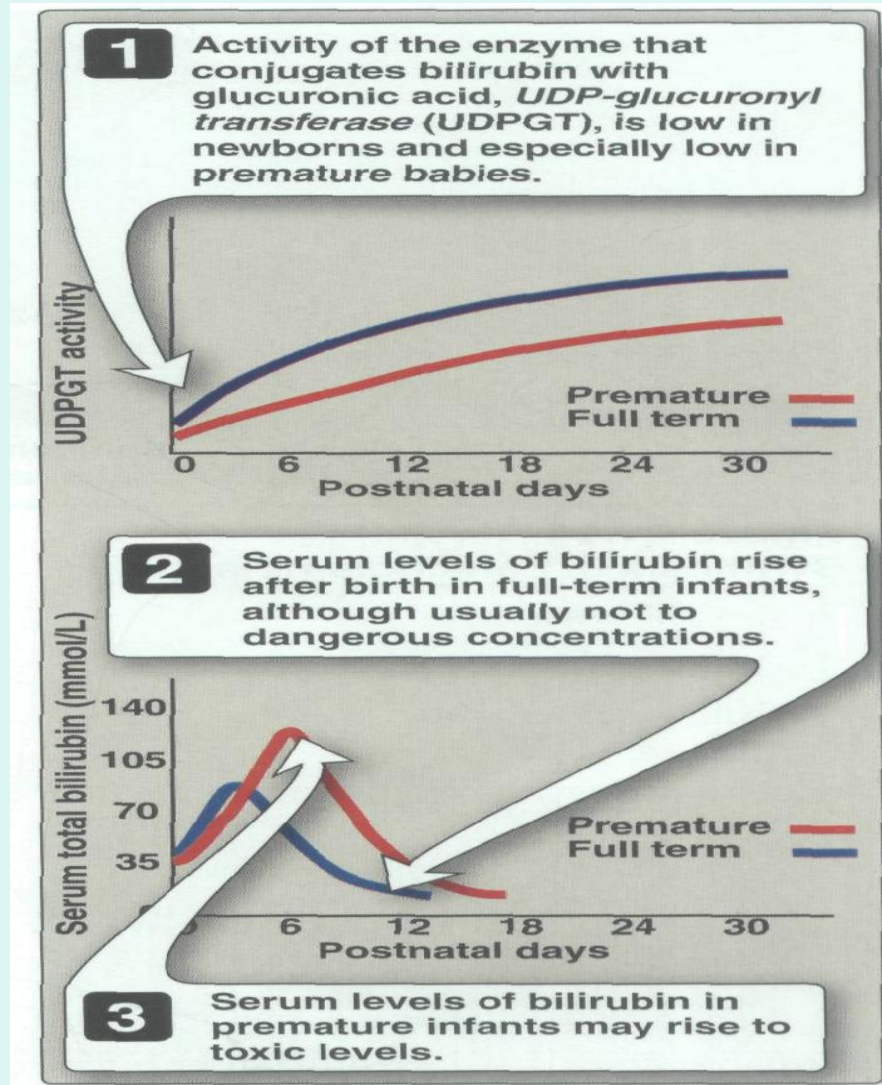


**Before
phototherapy**



**After
phototherapy**

Neonatal jaundice



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