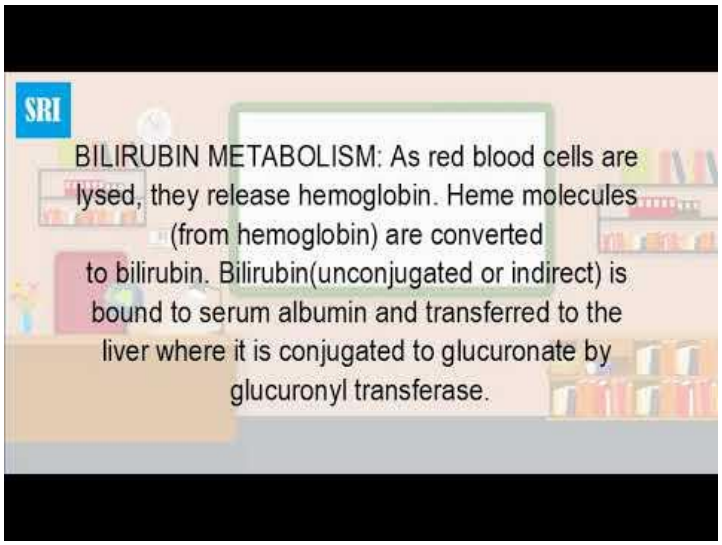
Bilirubin

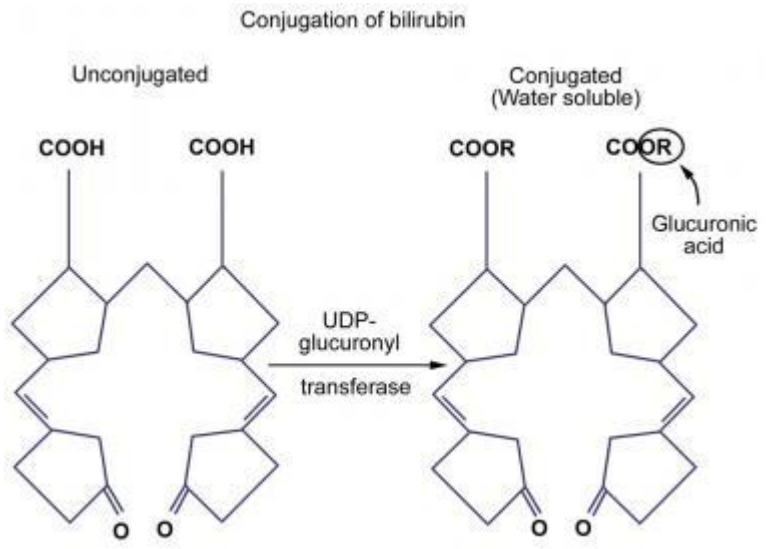
Define as a yellow compound result from normal catabolic pathway of heme after destruction of aged red blood cells.

Bilirubin is excreted in bile and urine, and elevated levels may indicate certain diseases.

It is responsible for the yellow color of bruises and the yellow discoloration in jaundice.

stercobilin, cause the brown color of faeces, **urobilin,** is the main component of the yellow color in urine.





Normal range:

bilirubin level found in the body reflects the balance between production and excretion.

- Direct (conjugated) bilirubin level = 0 - 0.3 mg/dl
– Total serum bilirubin level = 0.1 - 1.2 mg/dl

Population	Type of Bilirubin	Reference Range
Adults	Conjugated bilirubin	0.0–0.2 mg/dL (0–3 µmol/L)
	Unconjugated bilirubin	0.2–0.8 mg/dL (3–14 µmol/L)
	Total bilirubin	0.2–1.0 mg/dL (3–17 µmol/L)
Premature infants	Total bilirubin at 24 h	1–6 mg/dL (17–103 µmol/L)
	Total bilirubin at 48 h	6–8 mg/dL (103–137 µmol/L)
	Total bilirubin 3–5 d	10–12 mg/dL (171–205 µmol/L)
Full-term infants	Total bilirubin at 24 h	2–6 mg/dL (34–103 µmol/L)
	Total bilirubin at 48 h	6–7 mg/dL (103–120 µmol/L)
	Total bilirubin 3–5 d	4–6 mg/dL (68–103 µmol/L)

Catabolism of hemoglobin

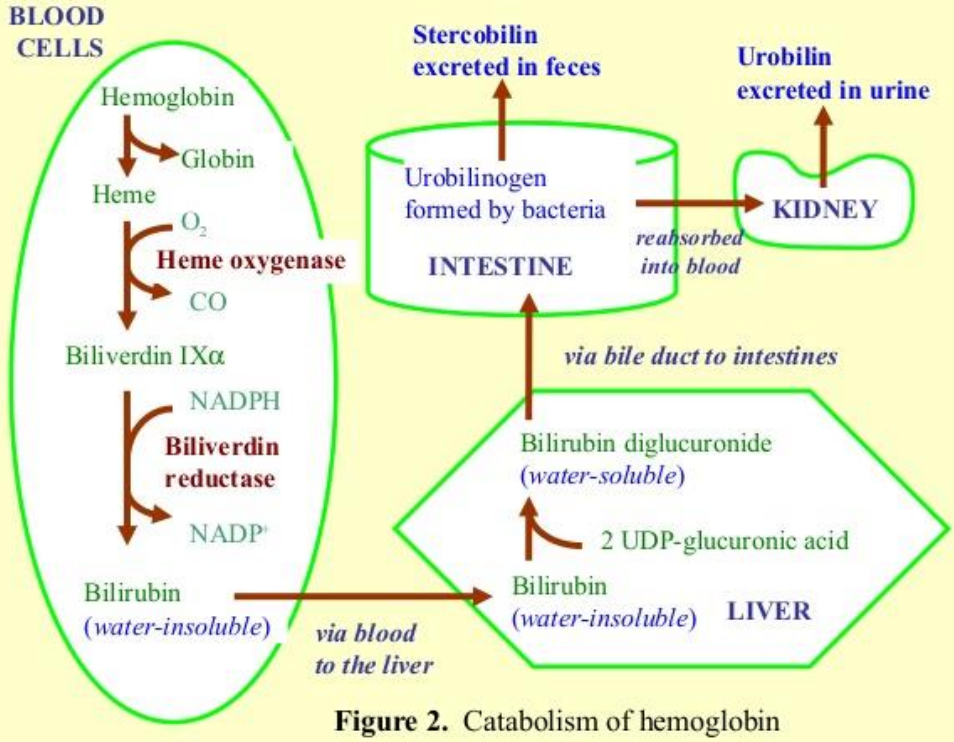


Figure 2. Catabolism of hemoglobin

Types of bilirubin in serum

- **Direct bilirubin:** is conjugated (water soluble bilirubin) in aqueous solution it reacts rapidly with reagent (direct reacting).
  Reference range: 0.0-0.2 mg/dL.

- **Indirect bilirubin:** is unconjugated (water insoluble bilirubin) because it is less soluble in it reacts more slowly with reagent (reaction carried out in methanol).
  Reference range: 0.2 -0.8 mg/dL.

- **Total bilirubin** = D+ ID.
  Reference range: 0.2 – 1.0 mg/dL.

Comparison between conjugated and unconjugated bilirubin

- Unconjugated bilirubin
  - Insoluble in blood
  - Largely attached to albumin in blood
  - Accumulates in pre-hepatic jaundice
  - Is toxic to tissues and organs such as the brain
  - Cannot be excreted in the urine
- Conjugated bilirubin
  - Is water soluble
  - Small amounts are loosely bound to albumin in blood
  - Accumulates in post-hepatic jaundice
  - Relatively non-toxic
  - Can be excreted in the urine

The fate of unconjugated bilirubin in liver:

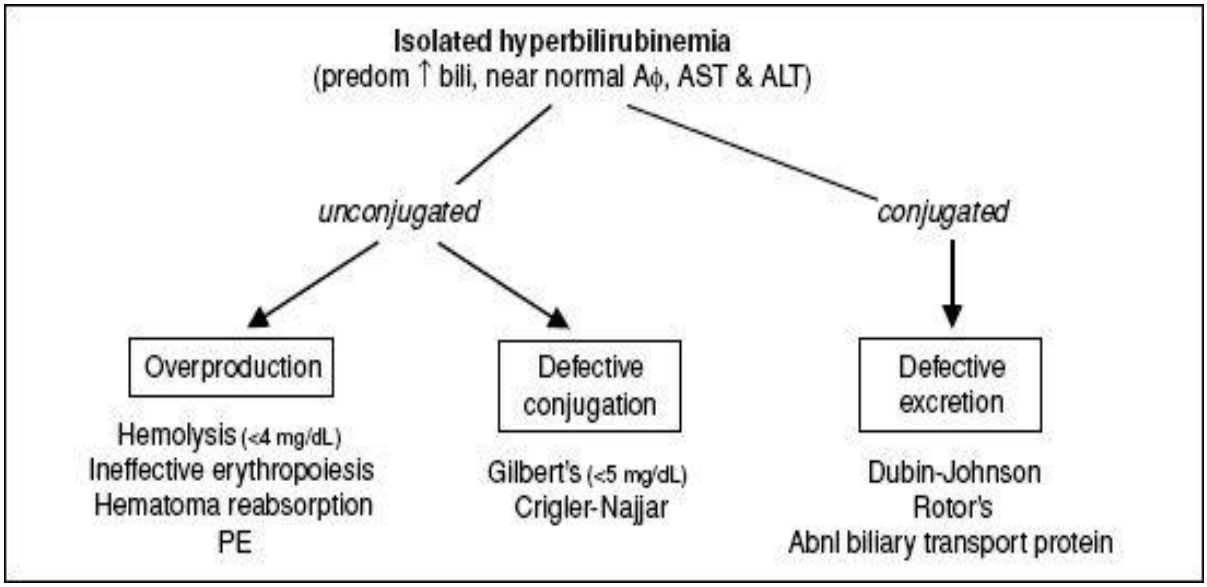
- Most of the bilirubin is chemically attached to a glucuronide before it is excreated in the bile . This conjugated bilirubin is called direct bilirubin (water soluble).

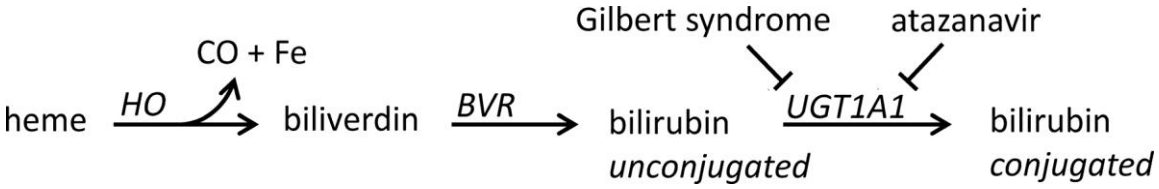
**The total bilirubin is equal direct bilirubin plus indirect bilirubin

- Conjecated bilirubin is excreated into blie by liver and stored in the gall bladder or transferred direct to small intestines.
- Bilirubin is further broken down by bacteria in intestine to urobilins ,,small amount of these compounds are reabsorbed and appear in

TABLE 5–16 • Causes of Elevations in Indirect and Direct Bilirubin Levels

Increased Indirect (Unconjugated) Bilirubin	Increased Direct (Conjugated) Bilirubin
Hemolysis: hemoglobinopathies, spherocytosis, G-6-PD deficiency, autoimmunity, transfusion reaction	Intrahepatic disruption: viral hepatitis, alcoholic hepatitis, chlorpromazine, cirrhosis Bile duct disease: biliary cirrhosis, cholangitis (idiopathic, infectious), biliary atresiaa
Red blood cell degradation: hemorrhage into soft tissues or body cavities, inefficient erythropoiesis, pernicious anemia	Extrahepatic bile duct obstruction: gallstones; carcinoma of gallbladder, bile ducts, or head of pancreas; bile duct stricture from inflammation or surgical misadventure
Defective hepatocellular uptake or conjugation: viral hepatitis, hereditary enzyme deficiencies (Gilbert, Crigler-Najjar syndromes), hepatic immaturity in newborns	





Jaundice, also known as **icterus**, is a yellowish or greenish pigmentation of the skin and whites of the eyes due to high bilirubin levels. It is commonly associated with itchiness. The feces may be pale and the urine dark.

Pathophysiology of jaundice:

1. Jaundice itself is not a disease, but rather a sign of one of many possible underlying pathological
2. When **red blood cells have completed their life span** of approximately 120 days, or when they are **damaged,** their membranes become fragile and rupture.

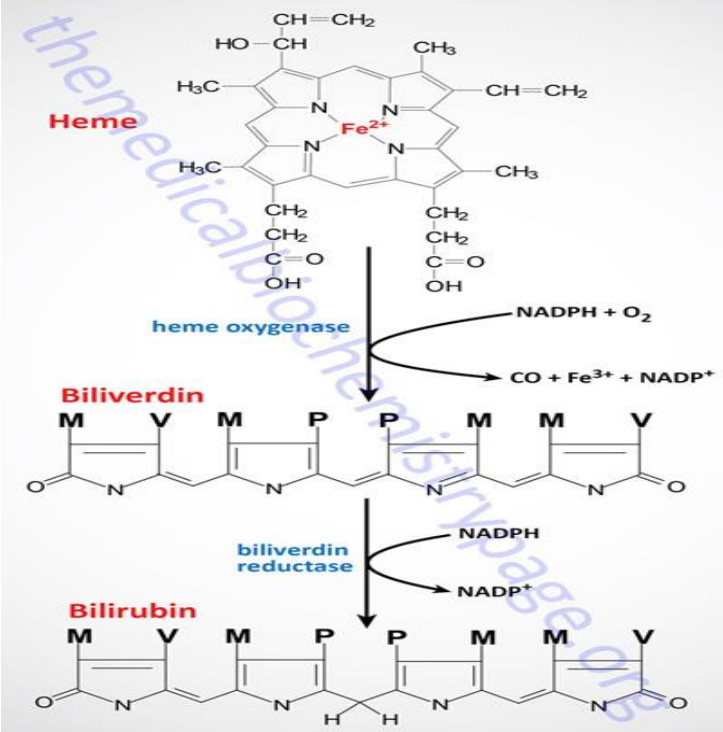
3. cellular contents, including hemoglobin, are released into the blood. The hemoglobin is phagocytosed by macrophages, and split into its heme and globin portions.
4. Two reactions then take place with the heme molecule.

The first oxidation reaction is catalyzed by the microsomal enzyme heme oxygenase and results in biliverdin (green color pigment), iron and carbon monoxide.

The next step is the reduction of biliverdin to a yellow color tetrapyrol pigment called bilirubin by biliverdin reductase.

This bilirubin is "unconjugated," "free" or "indirect" bilirubin. Approximately 4 mg of bilirubin per kg of blood is produced each day.

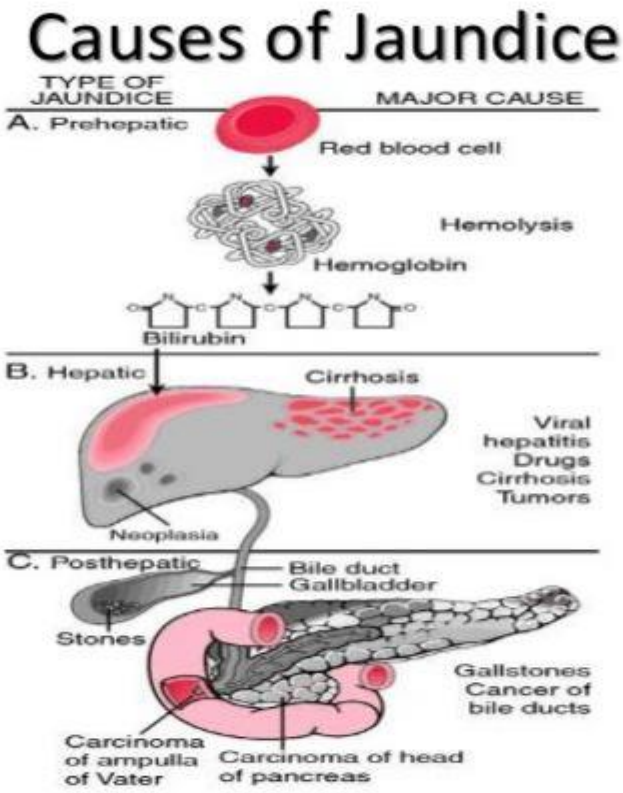
20 percent comes from other heme sources, including ineffective **erythropoiesis,** and the breakdown of other heme-containing proteins, such a muscle **myoglobin** and **cytochromes.**



Jaundice in babies occurs in over half in the first week following birth and in most is not a problem. If bilirubin levels in babies are very high for too long, a type of brain damage, known as **kernicterus,** may occur.

Normal levels of bilirubin in blood are below 1.0 mg /dL (17 µmol/L)

levels over 2–3 mg/dL (34-51 µmol /L) typically results in jaundice.



Symptomes

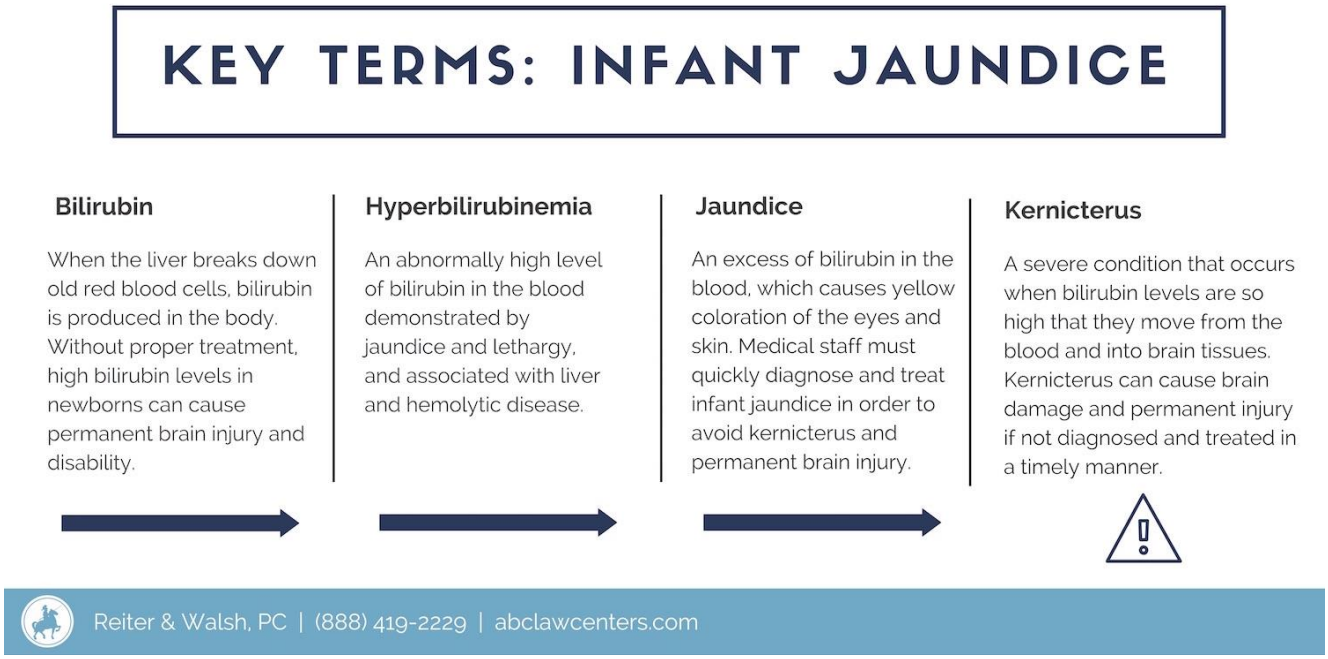
1. The main sign of jaundice is a yellowish discoloration of the white area of the eye and the skin.
2. Urine is dark color.
3. The presence of scleral icterus indicates a serum bilirubin of at least 3 mg /dL.
4. The conjunctiva of the eye are one of the first tissues to change yellowing color in jaundice.
5. The color of the skin and whites of the eyes will vary depending on levels of bilirubin.

Complications

hyperbilirubinemia due to accumulate of unconjugated bilirubin in the gray matter of the central nervous system, causing neurological damage leading to a condition known as **kernicterus.**

Depending on the level of exposure, the effects range from clinically unnoticeable to severe brain damage and even death.

Newborns are especially vulnerable to hyperbilirubinemia-induced neurological damage and therefore must be carefully monitored for alterations in their serum bilirubin levels.



Classification of Jaundice :

1. Pre hepatic jaundice:(unconjugated bilirubin)

a. hemolysis (breakdown of red blood cells).

b. severe malaria.

c. genetic diseases, such as sickle cell anemia, spherocytosis, thalassemia, pyruvate kinase deficiency, and glucose 6-phosphate dehydrogenase deficiency.

can lead to increased red cell lysis and therefore hemolytic jaundice

2. Hepatic jaundice: (conjugated bilirubin)

a. acute or chronic hepatitis, cirrhosis, drug-induced hepatitis, alcoholic liver disease

b. Cell necrosis reduces the liver's ability to metabolize and excrete bilirubin.

c. primary biliary cirrhosis (impairment of excretion of conjugated bilirubin into the Bile.

d. neonatal jaundice, is common in newborns: liver unable to conjugate and excretion of bilirubin,because liver does not fully mature until approximately two weeks of age.

e. Gilbert's syndrome and Crigler-Najjar syndrome (a genetic disorder of bilirubin metabolism which can result in mild jaundice).

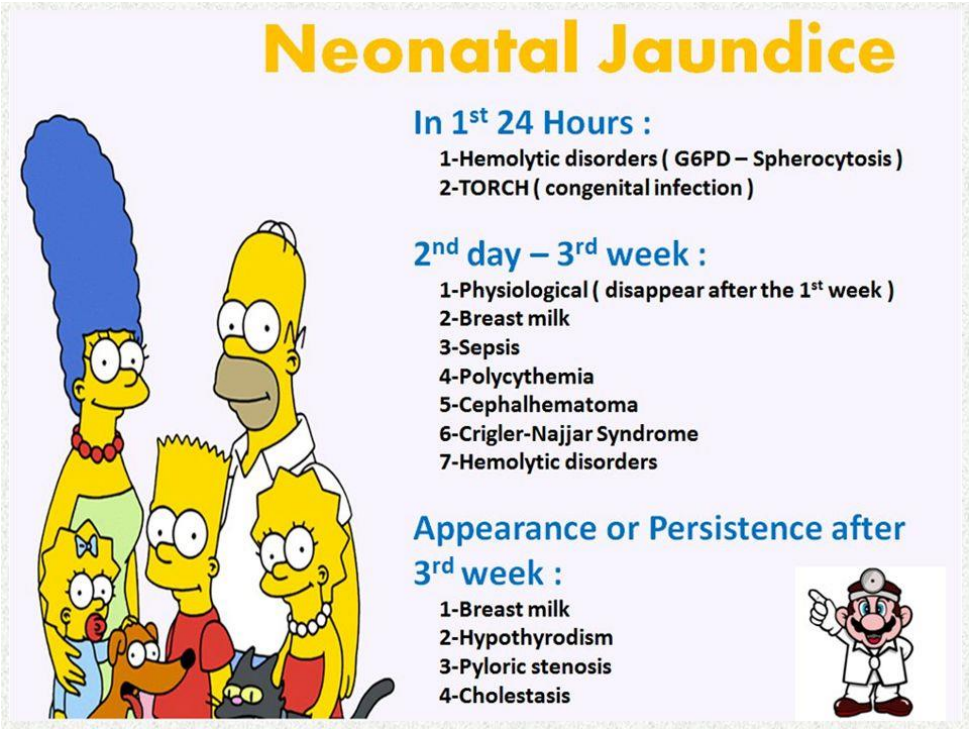
3. Post-hepatic jaundice, also called obstructive jaundice.

is caused by an interruption to the drainage of bile containing conjugated bilirubin in the biliary system.

1. **gallstones** in the common bile duct, and **pancreatic cancer in the head of the pancreas.**
2. **strictures of the common bile duct**, **biliary atresia**, **cholangio carcinoma**, **pancreatitis.**

Neonatal jaundice is usually harmless: this condition is often seen in infants around the second day after birth, lasting until day 8 in normal births, or to around day 14 in premature births. **hemolytic disorders include:**

1. **hereditary spherocytosis, glucose-6-phosphate dehydrogenase deficiency, pyruvate kinase deficiency**.
2. **ABO/Rh blood type autoantibodies.**
3. **infantile pyknocytosis**.



Treatment:

1. A Bili light used for early treatment, which often consists of exposing the baby to extensive phototherapy.
2. Sunbathing is effective treatment.
3. The advantage of ultra-violet-B, promotes Vitamin D production.
4. Bilirubin count is lowered through bowel movements and urination.
5. So frequent and effective feedings are especially important.]

Types of Jaundice

A. Physiological Jaundice

- Jaundice can be seen in 60% of Term infants & 80% of Preterm infants.
- It is mostly physiological

Features of physiological jaundice: (ALL of the following)

- Jaundice that first appears between 24-72 hours of age
- Maximum intensity is seen on 4-5th day in term and 7th day in preterm neonates
- Usually mild and less than 15mg/dl
- Clinically undetectable after 14 days

❖ Physiological jaundice is a diagnosis by exclusion.no treatment is required but baby should be observed closely for signs of worsening jaundice.

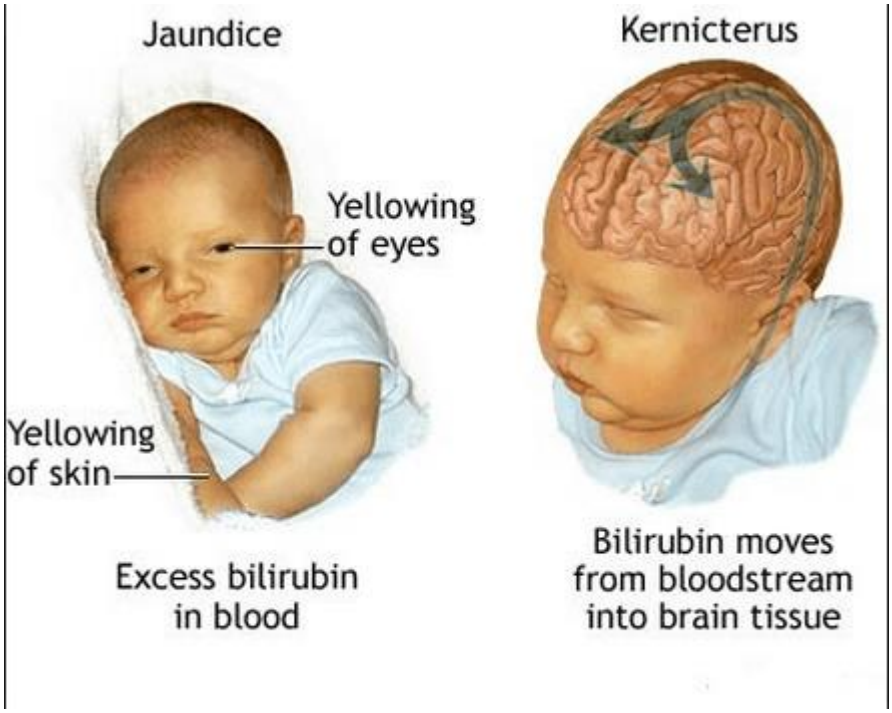
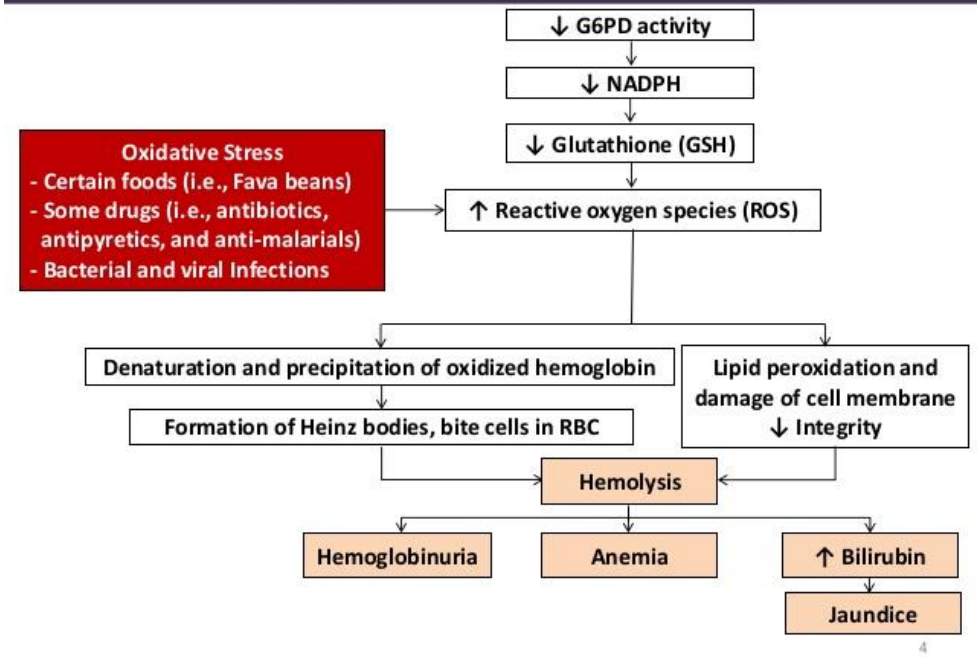
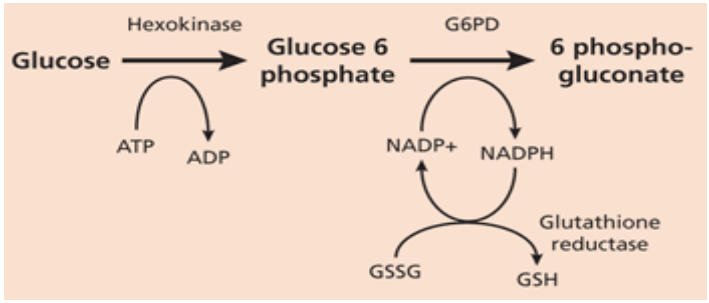


Table 1. Nonhemolytic Unconjugated Hyperbilirubinemia in the Neonatal Period.

Type of Disorder
1. Physiologic jaundice
2. Hereditary glucuronyl transferase deficiency
a) recessive
b) dominant
3. Transient familial neonatal hyperbilirubinemia
4. Breast-milk jaundice
5. Jaundice associated with high intestinal obstruction
6. Jaundice associated with hypothyroidism
7. Jaundice associated with novobiocin

Pathophysiology of G6PD deficiency



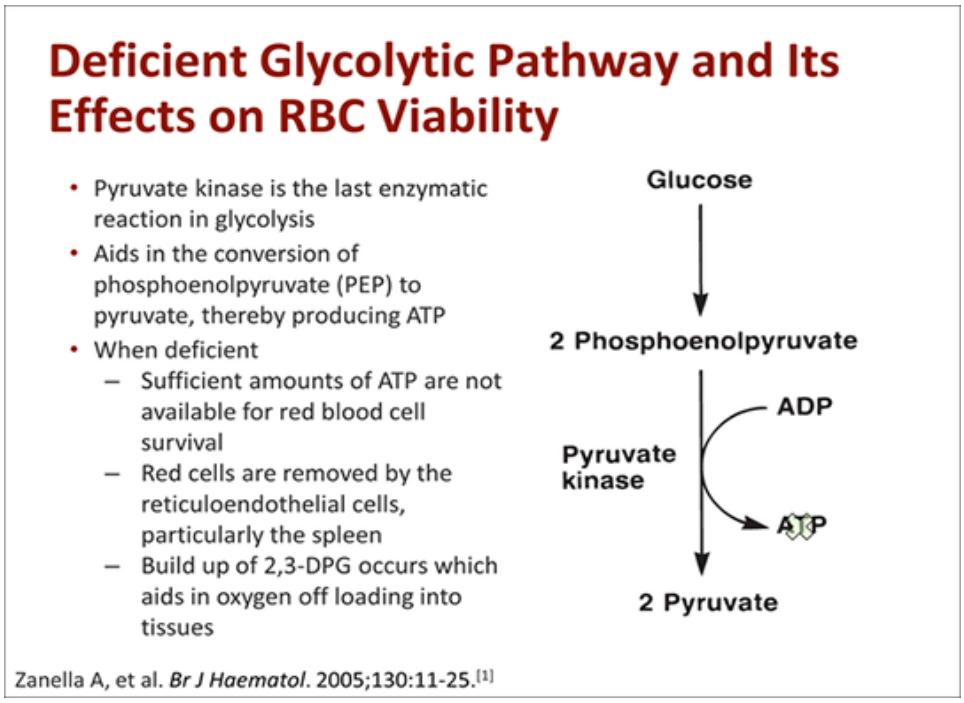


Introduction

- Glucose 6-phosphate dehydrogenase (G6PD) deficiency is an **inherited disease**
- This disease characterized by hemolytic anemia **caused by the inability to detoxify oxidizing agents**.
- G6PD deficiency is **X-linked**.
- Clinical manifestation of G6PD deficiency is **neonatal jaundice** appearing 1–4 days after birth.

Introduction

- G6PD deficiency is an allelic abnormality which is inherited in an X-linked recessive fashion.
- G6PD deficiency is also known as "favism" since G6PD deficient individuals are also sometimes allergic to fava beans.
- Glucose-6-Phosphate Dehydrogenase (G6PD) deficiency is the most common human enzyme deficiency in the world; it affects an estimated 400 million people.



When this occurs, the mother's blood cells develop antibodies that can attack the newborn's blood cells and **cause jaundice**. The risk of this is highest near or during delivery. **A-B-O incompatibility** occurs when: the mother is type O and the baby is B, A, or AB.

C. **ABO Incompatibility**. (1) Genetics: With maternal blood types A and B, isoimmunization does not occur because the naturally occurring antibodies (anti-A and -B) are IgM, not IgG. In type. O mothers, the antibodies are predominantly IgG, cross the placenta and can cause hemolysis in the fetus. The association of a type A ...

Diagnostic tests[20]			
Function test	**Pre-hepatic jaundice**	**Hepatic jaundice**	**Post-hepatic jaundice**
Alanine transferase(ALT) **aspartate transferase (AST) levels**	Normal	Increased	
Alkaline phosphatase levels	Normal	Increased	
Conjugated bilirubin	Normal	Increased	
Conjugated bilirubin in urine	Not present	Present	
Large spleen	Present	Present	Absent
Stool color	Normal	slightly pale	Pale
Total bilirubin	Normal / increased	Increased	
Unconjugated bilirubin	Normal / increased	Increased	Normal
Urine color	Normal[21]	Dark (urobilinogen + conjugated bilirubin)	Dark (conjugated bilirubin)

Diagnostic tests[20]			
Function test	**Pre-hepatic jaundice**	**Hepatic jaundice**	**Post-hepatic jaundice**
Urobilinogen	Normal / increased	Decreased	Decreased / negative

CLASSIFICATION OF JAUNDICE

PREDOMINANTLY UNCONJUGATED HYPERBILIRUBINEMIA

Excess production of bilirubin

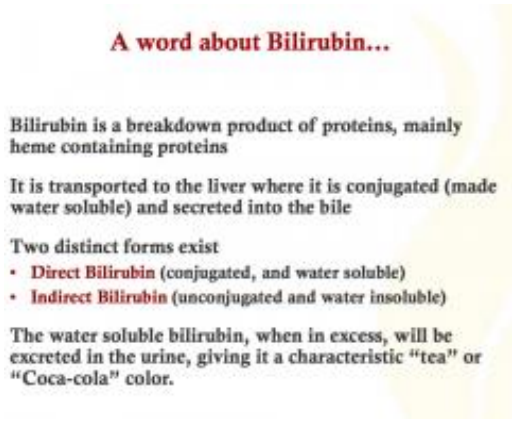
- Hemolytic anemias
- Resorption of blood from internal hemorrhage
  (e.g., alimentary tract bleeding, hematomas)
- Ineffective erythropoiesis syndromes
  (e.g., pernicious anemia, thalassemia)

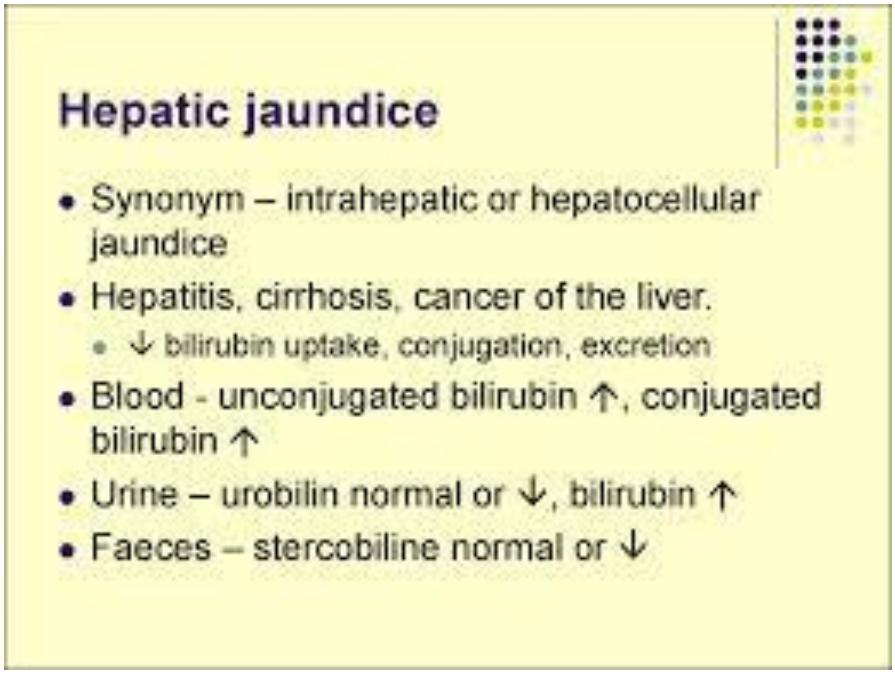
Reduced hepatic uptake

- Drug interference with membrane carrier systems
- Possibly some cases of Gilberts syndrome

Impaired bilirubin conjugation

- Physiologic jaundice of the newborn
  (decreased UGT activity, decreased excretion)
- Breast milk jaundice (?inhibition of UGT activity)
- Genetic deficiency of bilirubin UGT activity
  (Crigler-Najjar syndromes types I and II)
- Gilberts syndrome (apparently mixed etiologies)
- Diffuse hepatocellular disease
  (e.g., viral or drug-induced hepatitis, cirrhosis)

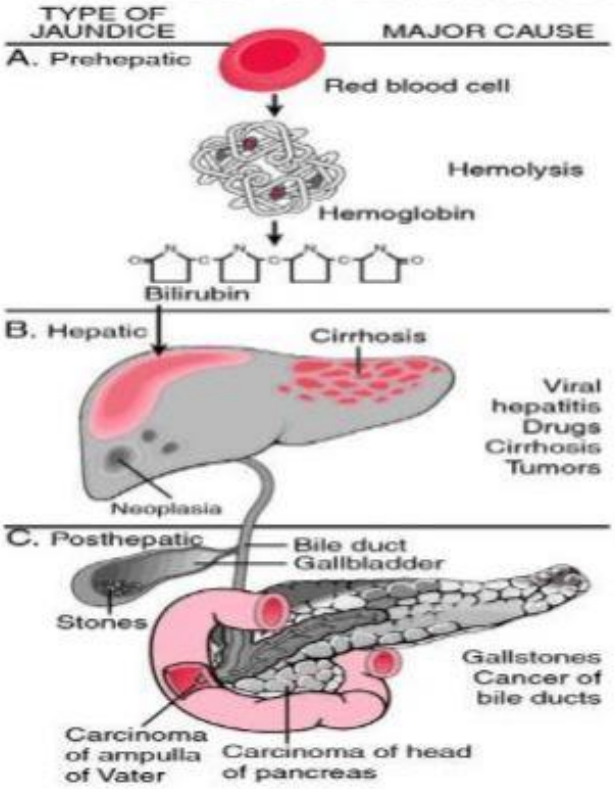




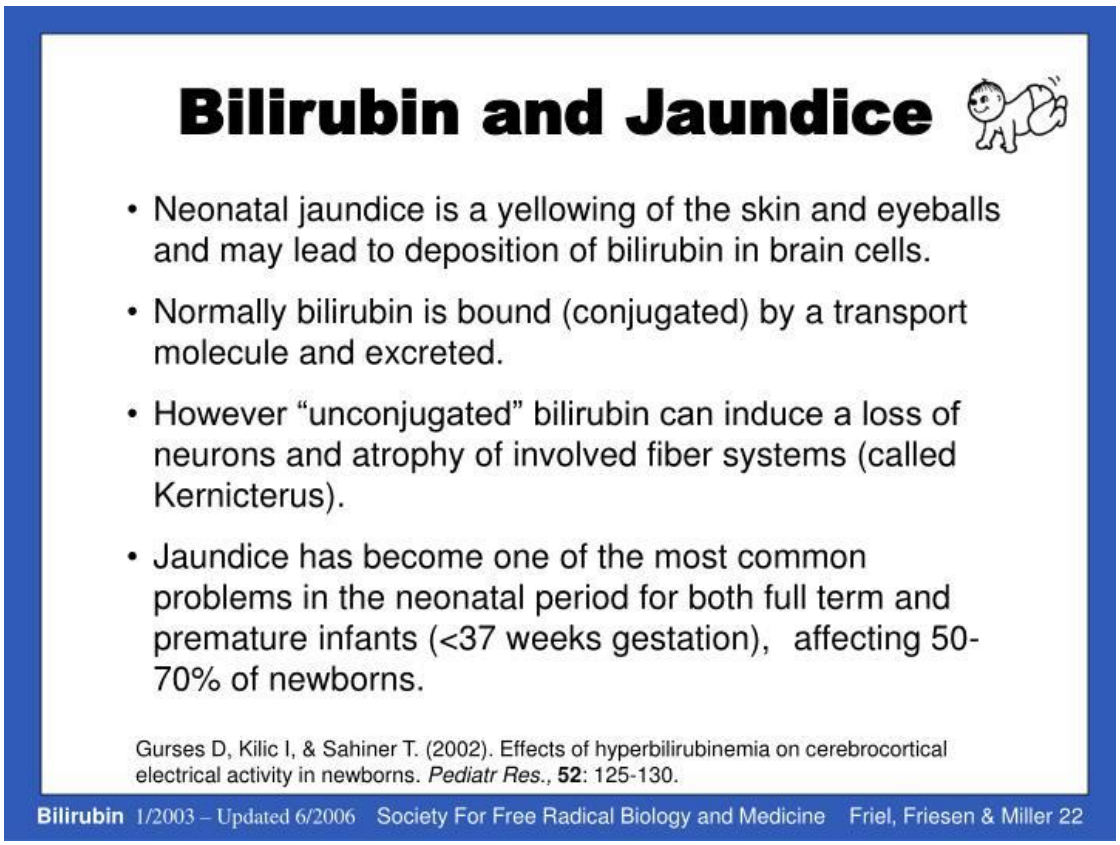
Types of Bilirubin

- Unconjugated bilirubin:
  - Insoluble in water.
  - Indirect bilirubin travels through the bloodstream to the liver, where it is changed into a soluble form (direct or conjugated).
- Conjugated bilirubin:
  - Soluble in water and is made by the liver from indirect bilirubin.

Causes of Jaundice



Increased erythrocyte breakdown	Decreased bilirubin clearance
Physiologic jaundice	Physiologic jaundice
Membrane conditions: spherocytosis, ellipsoidosis	Obstruction: biliary atresia, duodenal atresia
Infection: sepsis, CMV, TORCH	Breast milk jaundice
Enzyme defects: G6PD, pyruvate kinase deficiency	Liver enzyme defects: Gilbert syndrome, Crigler-Najjar syndrome
Globin synthesis defect: sickle cell, alpha-thalasemmia	Drug induced
Blood incompatibility: ABO, Rh	Liver disease: hepatitis, cirrhosis
Trauma	Metabolic: cystic fibrosis, galactosemia

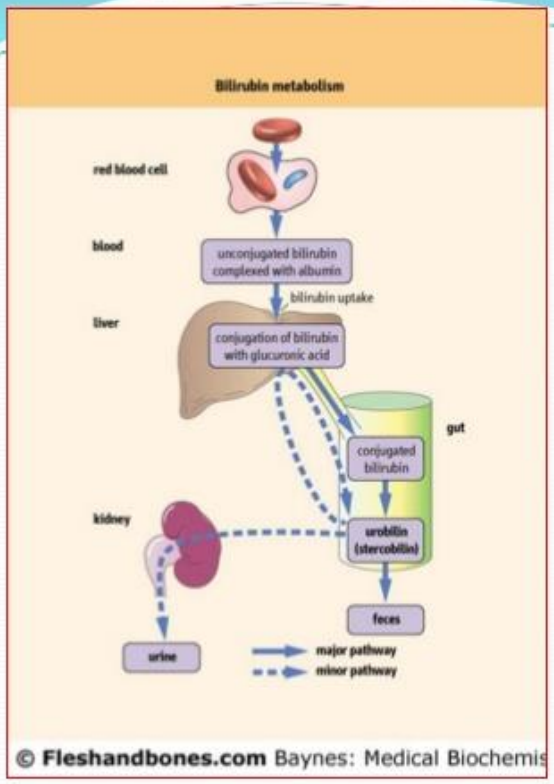


- Jaundice is one of the most common conditions needing medical attention in newborn babies. Approximately 60% of term and 80% of preterm babies develop jaundice in the first week of life, and about 10% of breastfed babies are still jaundiced at 1 month. For most babies, jaundice is not an indication of an underlying disease, and this early jaundice (termed 'physiological jaundice') is generally harmless.
- Jaundice has many possible causes, including blood group incompatibility, sepsis (infection), liver disease, bruising, metabolic disorders and deficiency of a particular enzyme, glucose-6-phosphate-dehydrogenase, can cause severe neonatal jaundice.
- Bilirubin travels in the blood in two ways; some is bound to albumin (a protein) and is called conjugated or direct bilirubin whereas the remainder is free, not bound, and is called unconjugated or indirect bilirubin.
- In young babies, unconjugated bilirubin can penetrate the blood–brain barrier. Unconjugated bilirubin is potentially toxic to neural tissue (brain and spinal cord). Entry of unconjugated bilirubin into the brain can cause both short-term and long-term neurological dysfunction.
- Clinical recognition and assessment of jaundice can be difficult. This is particularly so in babies with darker skin tones. Once jaundice is recognised, there is uncertainty about when to treat, and there is widespread variation in the use of phototherapy and exchange transfusion.
- This guideline provides guidance regarding the recognition, assessment and treatment of neonatal jaundice. The advice is based on evidence where this is available and on consensus-based practice where it is not.

Jaundice: the types

	Pre-hepatic Isolated **unconjugated Hyperbilirubinemia**	**Hepatocellular** **Mixed Hyperbilirubinemia**	**Post-hepatic** Predominantly **conjugated Hyperbilirubinemia**
Pathophysiology	Unconjugated bilirubin levels exceed liver's capacity to conjugate	Both Bilirubin uptake and conjugation impaired because of liver cell dysfunction	Liver conjugates normally but outflow of conjugated bilirubin is impaired
Causes	**Hemolysis** Congenital deficiency of enzyme Glucuronyl transferase e.g. in **Criggler-Najjar** and **Gilbert Syndromes**	Parenchymal Liver disease e.g. **hepatitis (viral and other), Wilson's disease, Hemochromatosis** etc.	**Stones in bile duct, tumor** blocking bile flow, **Dubin-Johnson and Rotor's Syndromes**

NORMAL BILIRUBIN METABOLISM



In liver unconjugated bilirubin is conjugated with glucoronic acid catalyzed by UDP glucuronyl tranferase

"Conjugated" bilirubin is water soluble and is secreted by the hepatocytes into the biliary canaliculi

Converted to urobilinogen (colorless) by bacteria in the gut

Oxidized to stercobilin which is colored and excreted in feces

Some stercobilin may be re-adsorbed by the gut and re-excreted by either the liver or kidney

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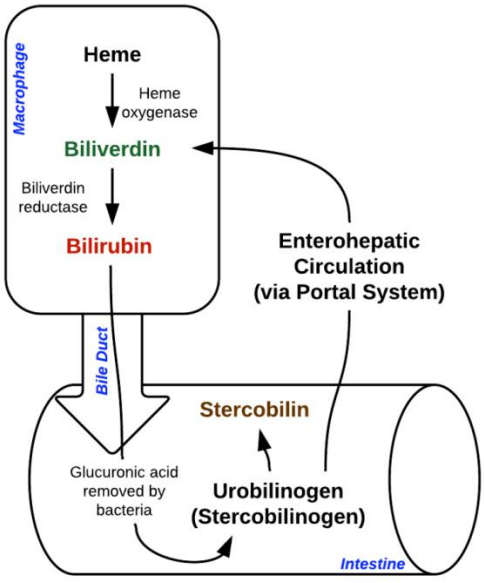

Hereditary Disorders of Bilirubin Metabolism

- Gilbert's syndrome (≤ 7% of population)
  - Autosomal dominant
  - Unconjugated hyperbilirubinemia
  - Deficiency of glucuronyl transferase and inadequate uptake of bilirubin
  - Result - - - - -> mild, no morbidity

- Dubin-Johnson syndrome
  - Autosomal recessive
  - Conjugated hyperbilirubinemia
  - Lack transport protein
  - Result - - - - -> enlarged and pigmented liver

- Crigler-Najjar syndrome
  - Autosomal recessive
  - Neonates
  - Complete absence of glucuronyl transferase
  - Result - - - – > ranges from yellow discoloration to death

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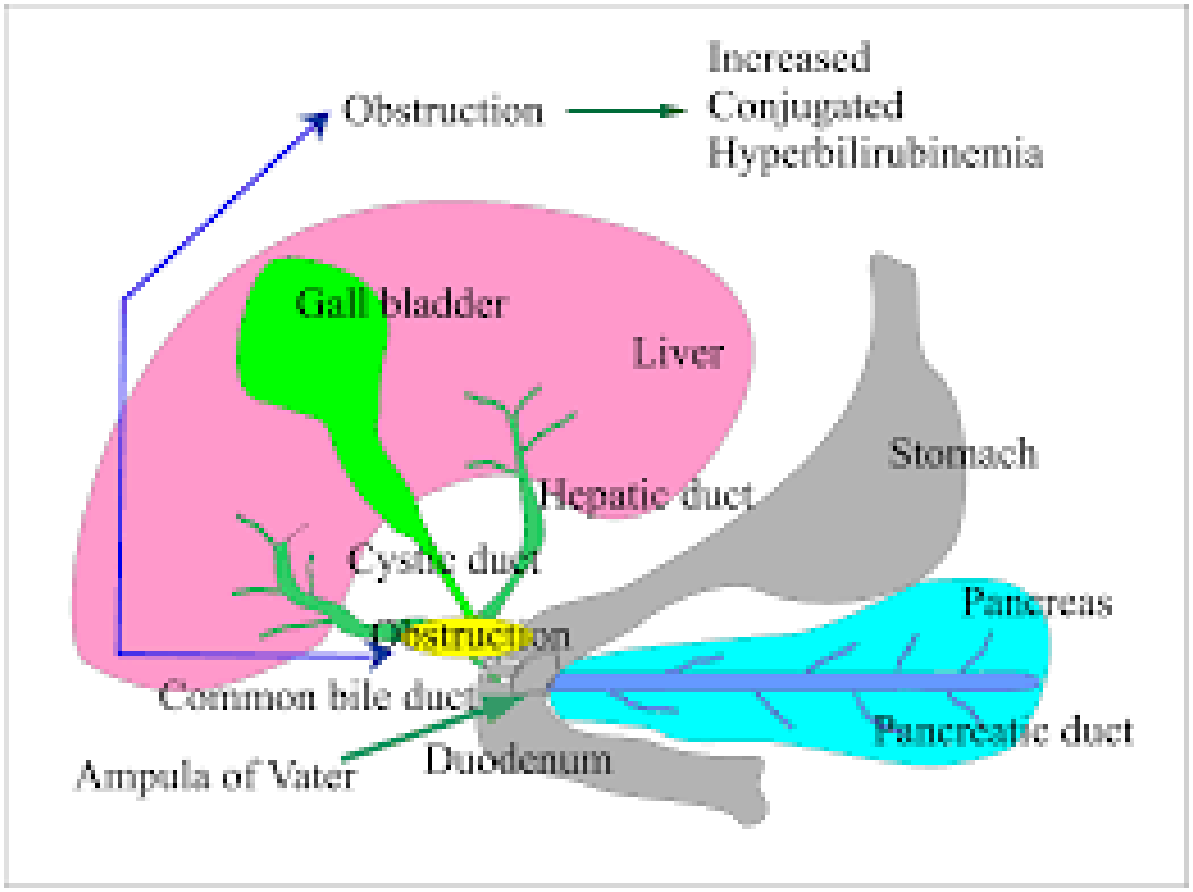
Jaundice; Hemolytic

- Caused by any intravascular or extravascular hemolytic anemia
- Initially causes unconjugated hyperbilirubinemia, but since liver is unaffected will gradually convert to conjugated hyperbilirubinemia
- Elevated urine urobilinogen

Causes of Hyperbilirubinemia in Newborns

- Increased Bilirubin Production
  - Hemolytic disease
    - Immune mediated (Rh alloimmunization, ABO incompatibility)
    - Heritable (spherocytosis, G6PD deficiency, pyruvate kinas deficiency)
  - Polycythemia
  - Extravasation of blood (cephalohematoma, intraventricular hemorrhage)
  - Sepsis with disseminated intravascular coagulation (DIC)
- Decreased Bilirubin Clearance
  - Prematurity
  - Increased enterohepatic circulation
    - Breast milk jaundice
    - Pyloric stenosis
    - Small or large bowel obstruction
  - Inborn errors of metabolism (Gilbert syndrome, Crigler-Najjar syndrome)
  - Metabolic discorder (hypothyroidism, hypopituitarism)



Population	Type of Bilirubin	Reference Range
Adults	Conjugated bilirubin	0.0–0.2 mg/dL (0–3 µmol/L)
	Unconjugated bilirubin	0.2–0.8 mg/dL (3–14 µmol/L)
	Total bilirubin	0.2–1.0 mg/dL (3–17 µmol/L)
Premature infants	Total bilirubin at 24 h	1–6 mg/dL (17–103 µmol/L)
	Total bilirubin at 48 h	6–8 mg/dL (103–137 µmol/L)
	Total bilirubin 3–5 d	10–12 mg/dL (171–205 µmol/L)
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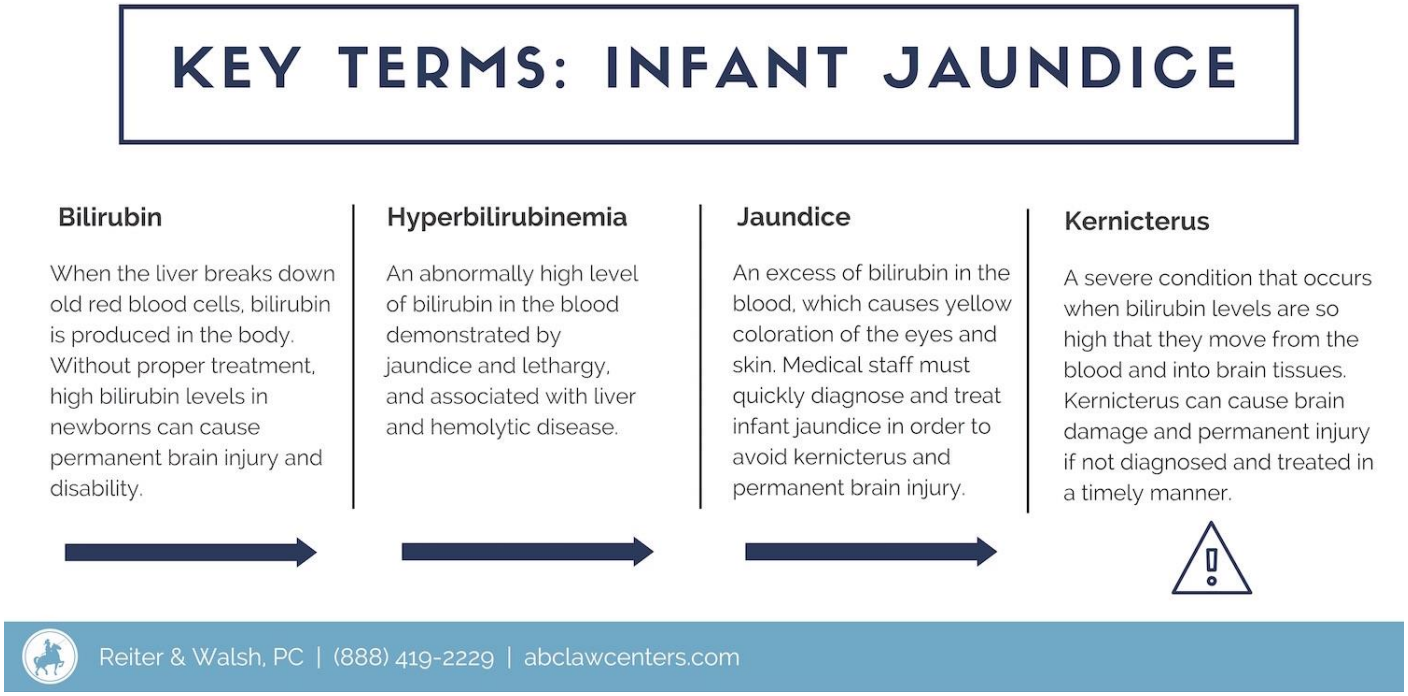
Comparison between conjugated and unconjugated bilirubin

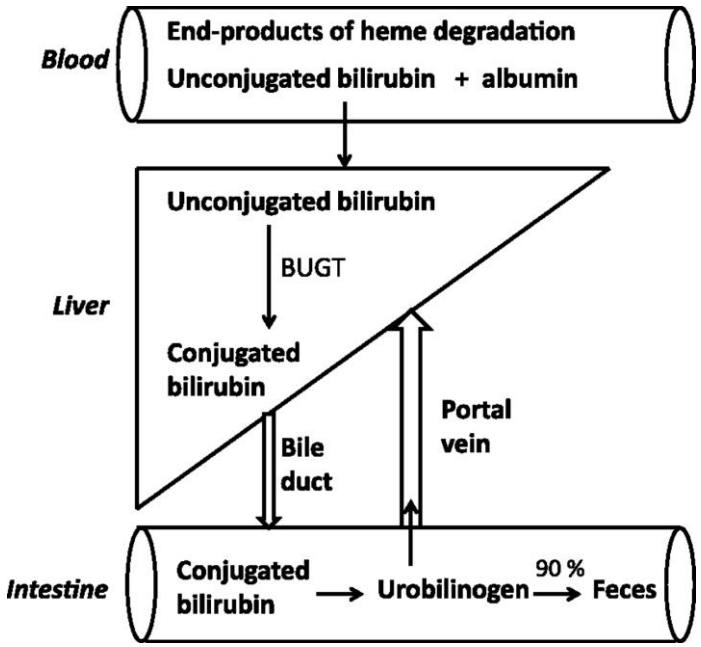
- Unconjugated bilirubin
  - Insoluble in blood
  - Largely attached to albumin in blood
  - Accumulates in pre-hepatic jaundice
  - Is toxic to tissues and organs such as the brain
  - Cannot be excreted in the urine
- Conjugated bilirubin
  - Is water soluble
  - Small amounts are loosely bound to albumin in blood
  - Accumulates in post-hepatic jaundice
  - Relatively non-toxic
  - Can be excreted in the urine



Bilirubin is a yellow-colored waste material that remains in the bloodstream after iron is removed from the blood.

The liver filters waste out from the blood. When bilirubin reaches the liver, other chemicals attach to it. A substance called conjugated bilirubin results.

The liver produces bile, a digestive juice. Conjugated bilirubin enters the bile, then it leaves the body. It is this type of bilirubin that gives feces its brown color.



Causes of neonatal jaundice

Unconjugated bilirubin level > 300μmol/L may be associated with Kernicterus (brain damage due to uptake of unconjugated bilirubin)

Causes of neonatal jaundice	
Unconjugated	Haemolytic disorders e.g. blood group incompatibility red cell enzyme deficiency Increased red cell mass e.g. placental or twin-twin transfusion Hypoxia Galactosaemia Fructosaemia Meconium retention Hereditary unconjugated hyperbilirubinaemias
Conjugated	Infections - bacterial or viral Biliary atresia Cryptogenic Genetic conditions - hereditary conjugated hyperbilirubinaemias Endocrine - hypothyroidism Chromosomal Vascular abnormalities Total parenteral nutrition

Unconjugated	Conjugated
Hemolytic anemias	Obstruction of the biliary tree
Neonatal "physiological jaundice"	Dubin–Johnson syndrome
Crigler–Najjar syndromes types I and II	Rotor syndrome
Gilbert syndrome	Liver diseases such as the various types of hepatitis
Toxic hyperbilirubinemia	

These causes are discussed briefly in the text. Common causes of obstruction of the biliary tree are a stone in the common bile duct and cancer of the head of the pancreas. Various liver diseases (eg, the various types of hepatitis) are frequent causes of predominantly conjugated hyperbilirubinemia.

Risk factors

Jaundice most often happens as a result of an underlying disorder that either causes the production of too much bilirubin or prevents the liver from getting rid of it. Both of these result in bilirubin being deposited in tissues.

Underlying conditions that may cause jaundice include:

- **Acute inflammation of the liver:** This may impair the ability of the liver to conjugate and secrete bilirubin, resulting in a buildup.
- **Inflammation of the bile duct:** This can prevent the secretion of bile and removal of bilirubin, causing jaundice.
- **Obstruction of the bile duct:** This prevents the liver from disposing of bilirubin.
- **Hemolytic anemia:** The production of bilirubin increases when large quantities of red blood cells are broken down.
- **Gilbert's syndrome:** This is an inherited condition that impairs the ability of enzymes to process the excretion of bile.
- **Cholestasis:** This interrupts the flow of bile from the liver. The bile containing conjugated bilirubin remains in the liver instead of being excreted.

Rarer conditions that may cause jaundice include:

- **Crigler-Najjar syndrome:** This is an inherited condition that impairs the specific enzyme responsible for processing bilirubin.
- **Dubin-Johnson syndrome:** This is an inherited form of chronic jaundice that prevents conjugated bilirubin from being secreted from of the cells of the liver.
- **Pseudojaundice:** This is a harmless form of jaundice. The yellowing of the skin results from an excess of beta-carotene, not from an excess of bilirubin. Pseudojaundice usually arises from eating large quantities of carrot, pumpkin, or melon.

Causes and treatments of infant jaundice

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By Caroline Gillott

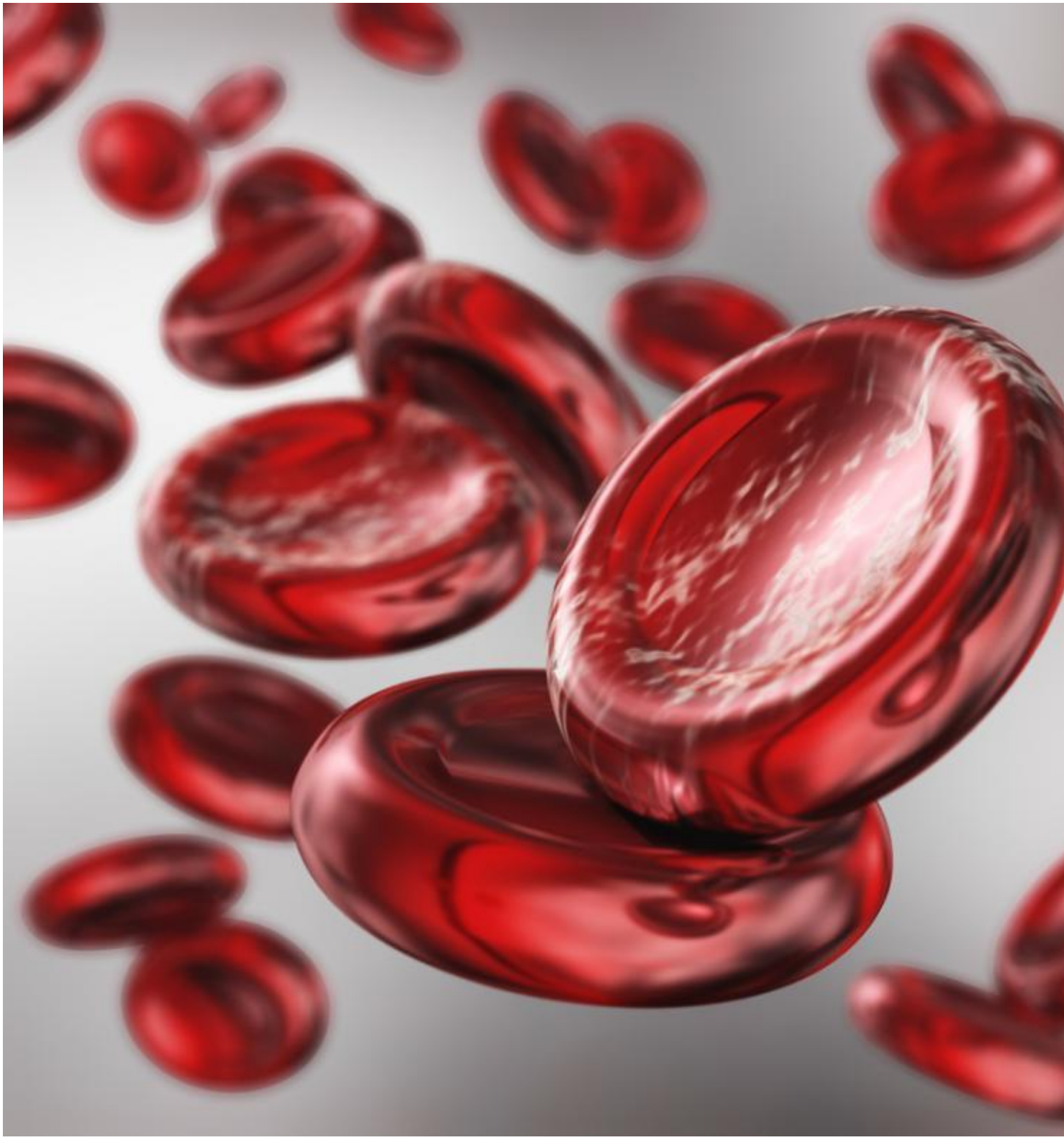
Reviewed by Karen Gill, MD

Infant jaundice is a condition where a baby's skin, and the white part of their eye, appear yellow. Jaundice is a common condition in infants, affecting over 50 percent of all newborns. Jaundice is particularly common in premature babies - boys more often than girls. It usually appears within the baby's first week of life.

In an otherwise healthy baby born at full term, infant jaundice is rarely a cause for alarm; it tends to go away on its own. However, if treatment is necessary, infants tend to respond to non-invasive therapy.

In rare cases, untreated infant jaundice may lead to brain damage and even death.

Causes



The cause of jaundice is excess bilirubin, a waste product produced when red blood cells are broken down.

Infant jaundice is caused by an excess of bilirubin. Bilirubin is a waste product, produced when red blood cells are broken down. It is normally broken down in the liver and removed from the body in the stool.

Before a baby is born, it has a different form of hemoglobin. Once they are born, they very rapidly break down the old hemoglobin. This generates higher than normal levels of bilirubin that must be filtered out of the bloodstream by the liver and sent to the intestine for excretion.

However, an underdeveloped liver cannot filter out the bilirubin as fast as it is being produced, resulting in hyperbilirubinemia (an excess of bilirubin).

Infant jaundice with breast-feeding is common. It occurs in newborns that are breast-fed in two separate forms:

- **Breast-feeding jaundice** - occurs in the first week of life, if the baby does not feed well, or if the mother's milk is slow to come in.
- **Breast milk jaundice** - this is due to how substances in the breast milk interfere with the breakdown process of bilirubin. It occurs after 7 days of life, peaking at 2-3 weeks.

Some cases of severe infant jaundice are linked to an underlying disorder; these include:

- liver disease
- sickle cell anemia
- bleeding underneath the scalp (cephalohematoma) - caused by a difficult delivery
- sepsis - a blood infection
- an abnormality of the baby's red blood cells
- blocked bile duct or bowel
- rhesus or ABO incompatibility - when the mother and baby have different blood types, the mother's antibodies attack the baby's red blood cells
- higher numbers of red blood cells - more common in smaller babies and twins
- enzyme deficiency
- bacterial or viral infections
- hypothyroidism - underactive thyroid gland
- hepatitis - an inflammation of the liver
- hypoxia - low oxygen levels
- some infections - including syphilis and rubella

Risk factors

Common risk factors for infant jaundice are:

- **Premature birth** - premature babies have severely underdeveloped livers and fewer bowel movements, this means there is a slower filtering and infrequent excretion of bilirubin.

- **Breast-feeding** - babies who do not get enough nutrients or calories from breast milk or become dehydrated are more likely to develop jaundice.
- **Rhesus or ABO incompatibility** - when a mother and baby have different blood types, the mother's antibodies go through the placenta and attack the red blood cells of the fetus, causing accelerated break down.
- **Bruising during birth** - this can make red blood cells break down faster, resulting in higher levels of bilirubin.

Symptoms

The most pervasive sign of infant jaundice is yellow skin and sclerae (the whites of the eyes). This typically starts at the head, and spreads to the chest, stomach, arms, and legs.

Symptoms of infant jaundice can also include:

- drowsiness
- pale stools - breast-fed babies should have greenish-yellow stools, while those of bottle fed babies should be a greenish-mustard color
- poor sucking or feeding
- dark urine - a newborn's urine should be colorless

Symptoms of severe infant jaundice include:

- yellow abdomen or limbs
- drowsiness
- inability to gain weight
- poor feeding
- irritability

Diagnosis

Doctors recommend that babies be tested for jaundice before being discharged from the hospital and again 3-5 days after birth, when bilirubin levels are highest.

Doctors will most likely diagnose jaundice based on appearance alone. However, the severity of jaundice will be determined by measuring levels of bilirubin in the blood. Bilirubin levels can be checked via a serum bilirubin (SBR) blood test or a transcutaneous bilirubinometer device, which measures how much of a certain light shines through the skin.

If the infant's jaundice persists for more than 2 weeks, doctors may perform further blood tests and urine tests to check for underlying disorders. However, in breast-fed babies who are otherwise well and feeding and gaining weight appropriately, this can be normal.

Treatment

Phototherapy, pictured here, is a treatment for cases of infant jaundice that do not resolve on their own.

Typically, treatment for mild jaundice in infants is unnecessary, as it tends to disappear on its own within 2 weeks.

If the infant has severe jaundice, they may need to be readmitted to the hospital for treatment to lower levels of bilirubin in the bloodstream. In some less severe cases, treatment may be done at home.

Some treatment options for severe jaundice include:

- **Phototherapy (light therapy)** - treatment by light rays. The baby is put under a special light, covered by a plastic shield to filter out ultraviolet light. The light manipulates the structure of bilirubin molecules so they can be excreted.
- **Exchange blood transfusion** - the baby's blood is repeatedly withdrawn and then replaced (exchanged) with donor blood. This procedure will only be considered if phototherapy does not work because the baby would need to be in an intensive care unit (ICU) for newborns.
- **Intravenous immunoglobulin (IVIg)** - in cases of rhesus or ABO incompatibility, the infant may have a transfusion of immunoglobulin; this is a protein in the blood that lowers the levels of antibodies from the mother, which are attacking the infant's red blood cells.

If jaundice is caused by something else, surgery or drug treatment may be required.

Complications

Untreated jaundice may lead to complications.

- **Acute bilirubin encephalopathy**: A condition caused by a build-up of bilirubin in the brain (bilirubin is toxic to brain cells). Signs of acute bilirubin encephalopathy in a baby with jaundice include fever, sluggishness, high-pitched crying, poor feeding, and arching of the body or neck. Immediate treatment may prevent further damage.
- **Kernicterus (nuclear jaundice)**: A potentially fatal syndrome that occurs if acute bilirubin encephalopathy causes permanent brain damage.

Other serious, but rare complications include deafness and cerebral palsy.

Prevention

The best way of reduce chances of an infant developing jaundice is to make sure they are well fed. For the first week or so of life, breast-fed babies should be fed 8-12 times a day, while formula-fed babies should be fed 1-2 ounces of formula every 2-3 hours.