

Bilirubin Metabolism

By

Aseel .j.abdullah

Introduction

- Bilirubin is the orange-yellow pigment derived from senescent red blood cells.
- It is a toxic waste product in the body.
- It is extracted and biotransformed mainly in the liver, and excreted in bile and urine.
- It is a bile pigment
- Elevations in serum and urine bilirubin levels are normally associated with Jaundice.

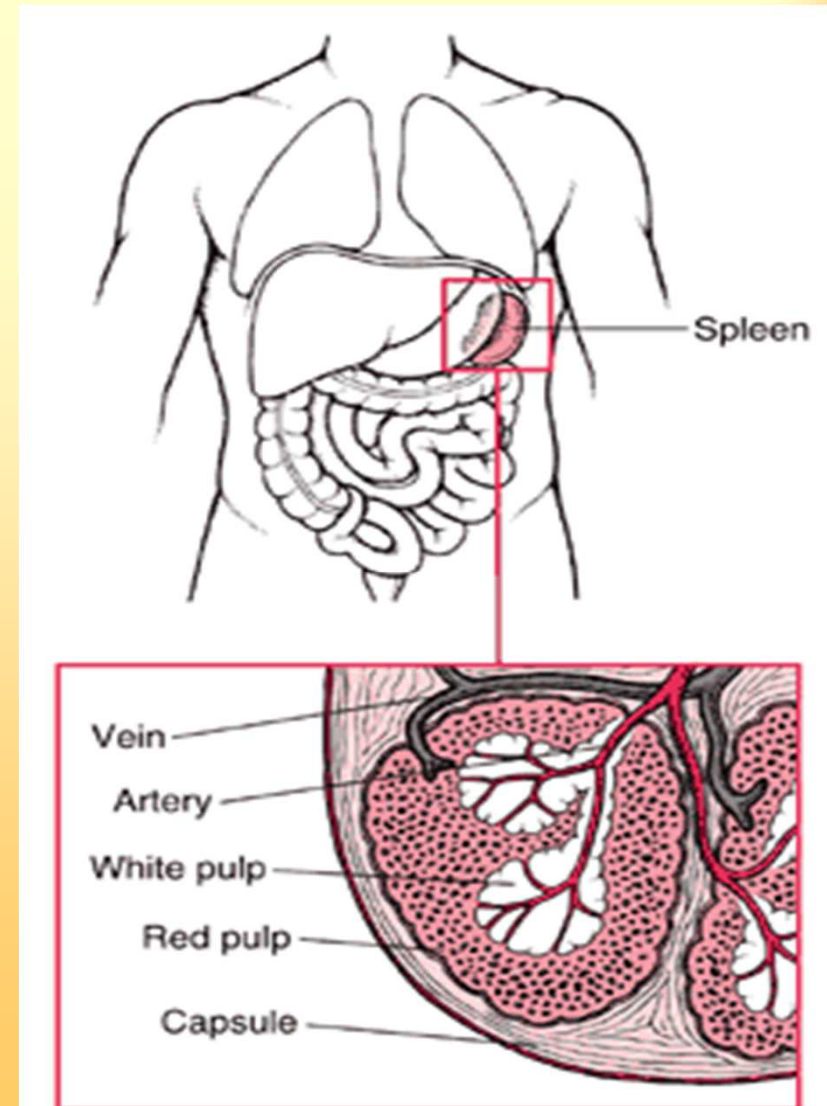
Erythrocytes become “old” as they lose their flexibility and increasingly rigid and fragile, they easily destruct during passage through tight circulation spots, especially in spleen, where the intra-capillary space is about 3 micron as compared to 8 micron of cell size

RBCs useful life span is 100 to 120 days, After which they become trapped and fragment in smaller circulatory channels, particularly in those of the spleen. For this reason, the spleen is sometimes called the “red blood cell graveyard.”

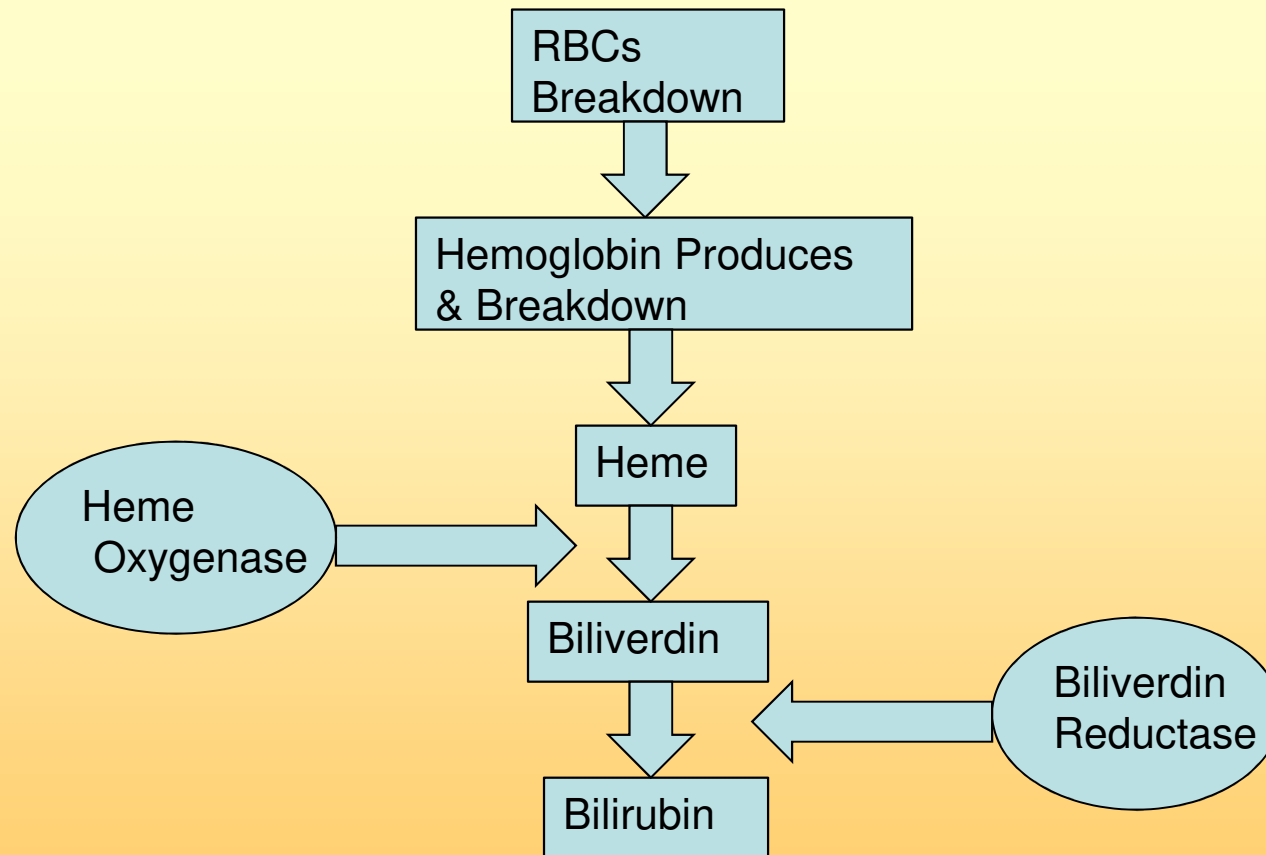
Dying erythrocytes are engulfed and destroyed by macrophages.

Formation of Bilirubin

- Primary site of synthesis:-
SPLEEN: The Graveyard
of Red Blood Cells
- Secondary site of synthesis:-
LIVER & BONE MARROW



Pathophysiology



In Blood

- The bilirubin synthesized in spleen, liver & bone marrow is unconjugated bilirubin.
- It is hydrophobic in nature so it is transported to the liver as a complex with the plasma protein, albumin.

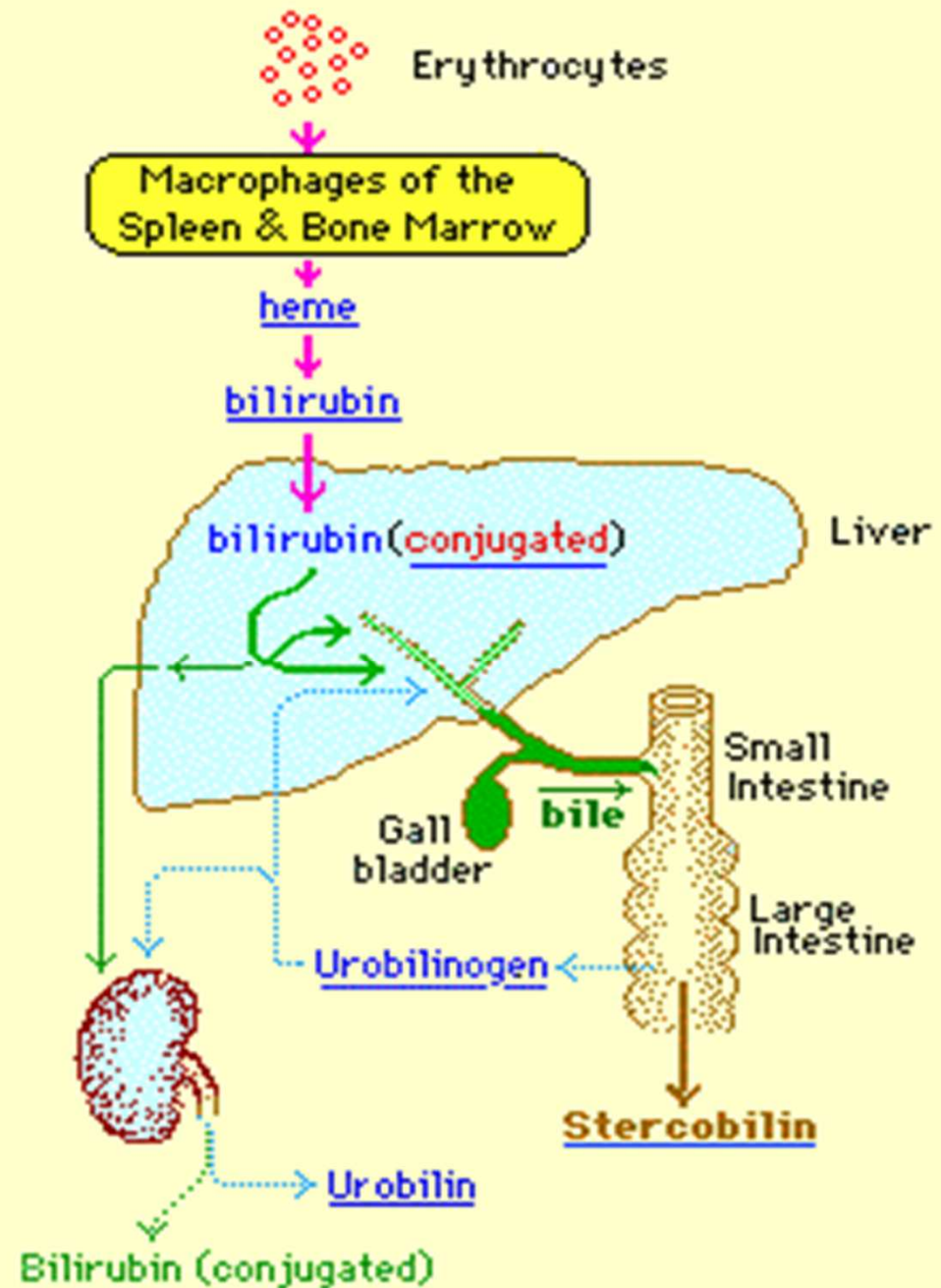
Unconjugated bilirubin

- Lipid soluble
- : limits excretion
- 1 gm albumin binds 8.5 mg bilirubin
- Fatty acids & drugs can displace bilirubin
- Indirect positive reaction in van den Bergh test

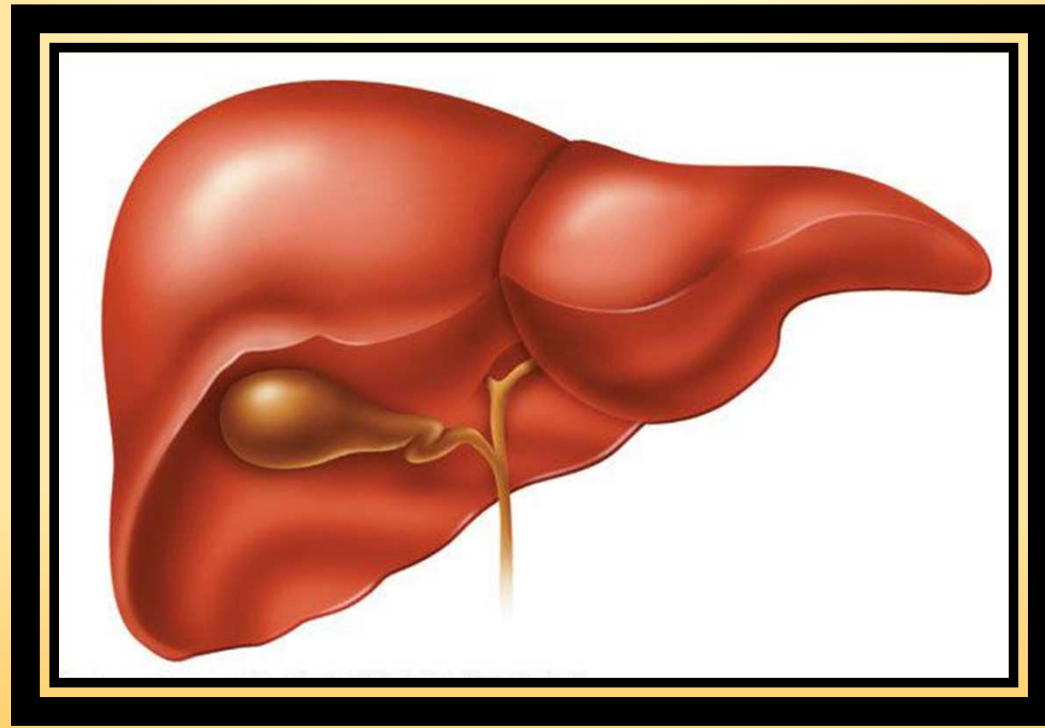
- Most of the reabsorbed urobilinogen is taken up by the liver & is re-excreted in the bile.
- A small fraction (2 % - 5 %) enters the general circulation & appears in the urine.
- In the lower intestinal tract, the 3 urobilinogens spontaneously oxidize to produce the corresponding bile pigments;
 - Stercobilin
 - Mesobilin &
 - Urobilin;which are orange-brown in color and are the major pigments of stool.

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JAUNDICE



Clinical Significance

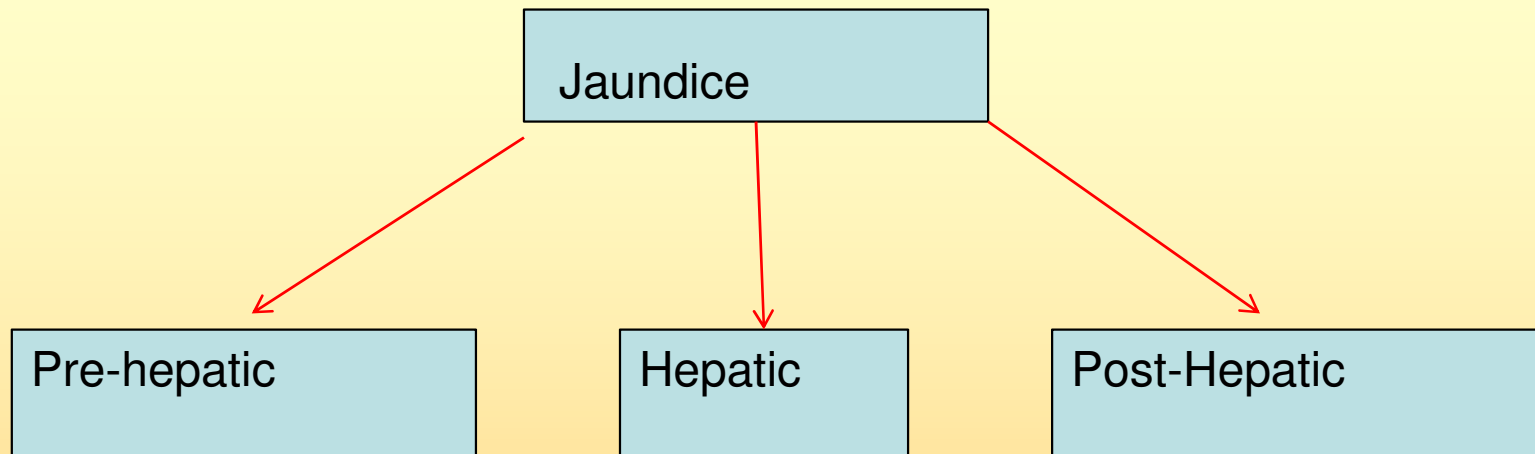
Hyperbilirubinemia & Types of Jaundice

- Hyperbilirubinemia : Increased plasma concentrations of bilirubin (> 3 mg/dl) occurs when there is an imbalance between its production and excretion.
- Recognized clinically as jaundice.
- Also known as icterus, a yellow discoloration of the skin, sclerae and mucous membrane.

- Jaundice becomes clinically evident when the serum bilirubin level exceeds 2.5mg/dL.
- Several types of Jaundice:
 - Hemolytic
 - Hepatocellular
 - Obstructive
- Symptoms:
 - Yellow discoloration of the skin, sclerae and mucous membranes
 - Itching (pruritus) due to deposits of bile salts on the skin
 - Stool becomes light in color
 - Urine becomes deep orange and foamy



Classification



The causes of jaundice

Type	Cause	Clinical example	Frequency
Prehepatic	hemolysis	autoimmune abnormal hemoglobin	uncommon depends on region
	infection	hepatitis A, B, C	common/very common
	chemical/drug	acetaminophen alcohol	common common
Intrahepatic	genetic errors: bilirubin metabolism	Gilbert's syndrome	1 in 20
		Crigler-Najjar syndrome	very rare
		Dubin-Johnson syndrome	very rare
		Rotor's syndrome	very rare
	genetic errors: specific proteins	Wilson's disease α_1 antitrypsin	1 in 200 000 1 in 1000 with genotype
Posthepatic	autoimmune	chronic active hepatitis	uncommon/ rare
	neonatal	physiologic	very common
	intrahepatic bile ducts	drugs primary biliary cirrhosis cholangitis	common uncommon common
extrahepatic bile ducts	gall stones pancreatic tumor cholangiocarcinoma	very common uncommon rare	

Neonatal Jaundice

- Common, particularly in premature infants.
- Transient (resolves in the first 10 days).
- Due to immaturity of the enzymes involved in bilirubin conjugation.
- High levels of unconjugated bilirubin are toxic to the newborn – due to its hydrophobicity it can cross the blood-brain barrier and cause a type of mental retardation known as kernicterus
- If bilirubin levels are judged to be too high, then phototherapy with UV light is used to convert it to a water soluble, non-toxic form.

Thank You