Physiology Team

LECTURE 9

Causes and Pathogenesis of Jaundice

GASTOINTISTINAL TRACT

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OBJECTIVES

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At the end of this lecture, student should be able to describe:

- Definition of Jaundice.
- The normal plasma concentration of total bilirubin.
- Classification of jaundice:
  - Prehepatic (hemolytic) jaundice
  - Hepatic (hepatocellular) jaundice
  - Posthepatic (obstructive) jaundice
- Neonatal Jaundice.

MIND MAP

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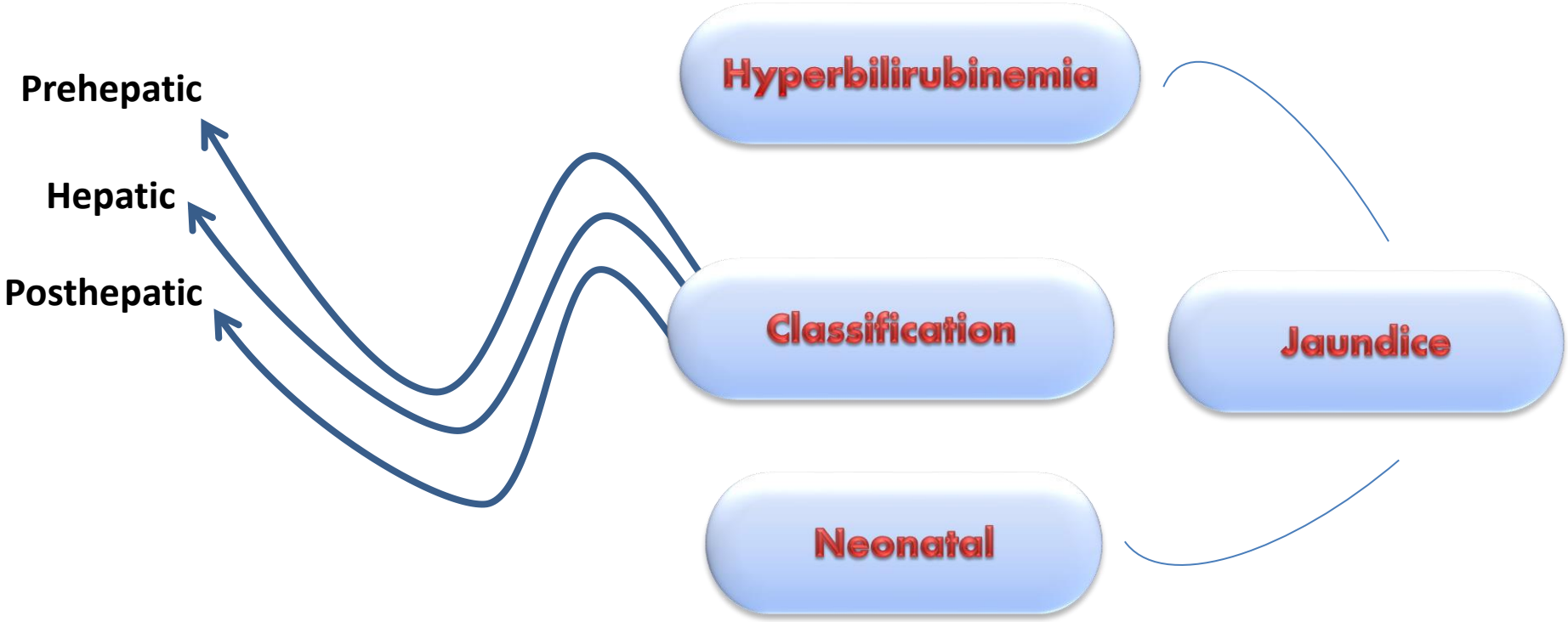

Causes and Pathogenesis of Jaundice:

Hyperbilirubinemia (Jaundice, Icterus):

- **Jaundice :** It is the yellow coloration of the skin, sclera, mucous membranes and deep tissues.

•The usual cause is **large** quantities of bilirubin in the **ECF**, either free or conjugated bilirubin.

•The **normal** plasma concentration of total bilirubin is **0.5** mg/dl.(0.3-1.2 mg/dl of blood)

•However, in certain **abnormal** conditions this can **rise up** to 40 mg/dl.

•The skin usually **begins to appear** jaundiced when the concentration of total bilirubin in the plasma is **greater than 2** mg/dl (34 µmol/l). **(clinical)**

•Bilirubin level from **0.5 to 2** mg/dl is called **subclinical** jaundice. **(has jaundice but can't be seen).**

Classification of jaundice:

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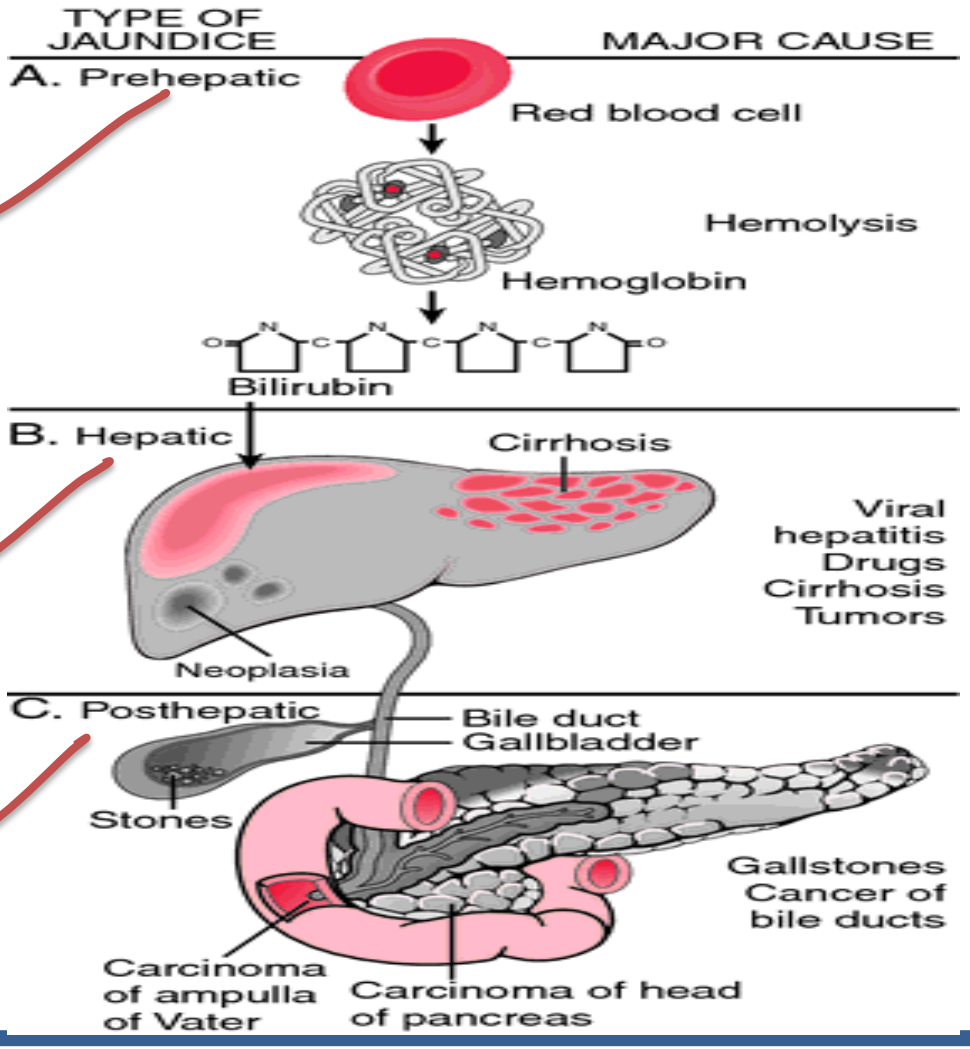
Prehepatic (hemolytic) jaundice

Hepatic (hepatocellular) jaundice

Poshepatic (obstructive) jaundice



Prehepatic (hemolytic) Jaundice , liver is not impaired

causes	Plasma bilirubin	Urine bilirubin	Van der Bergh reaction	Stools color
• It results from excess production of bilirubin (beyond the livers ability to conjugate it) following hemolysis. • Excess RBC lysis is commonly the result of: 1- Autoimmune disease 2- Hemolytic disease of the newborn 3- Rh- or ABOincompatibility 4- Structurally abnormal RBCs (Sickle cell disease) 5- Breakdown of extravasated blood	plasma concentrations of free bilirubin (hemobilirubin) rises to levels much above normal but it is not filtered through the kidney.	urine is free from bilirubin (**acholuric jaundice**).	indirect	The stools appear darker than the normal color due to excessive stercobilin formation.

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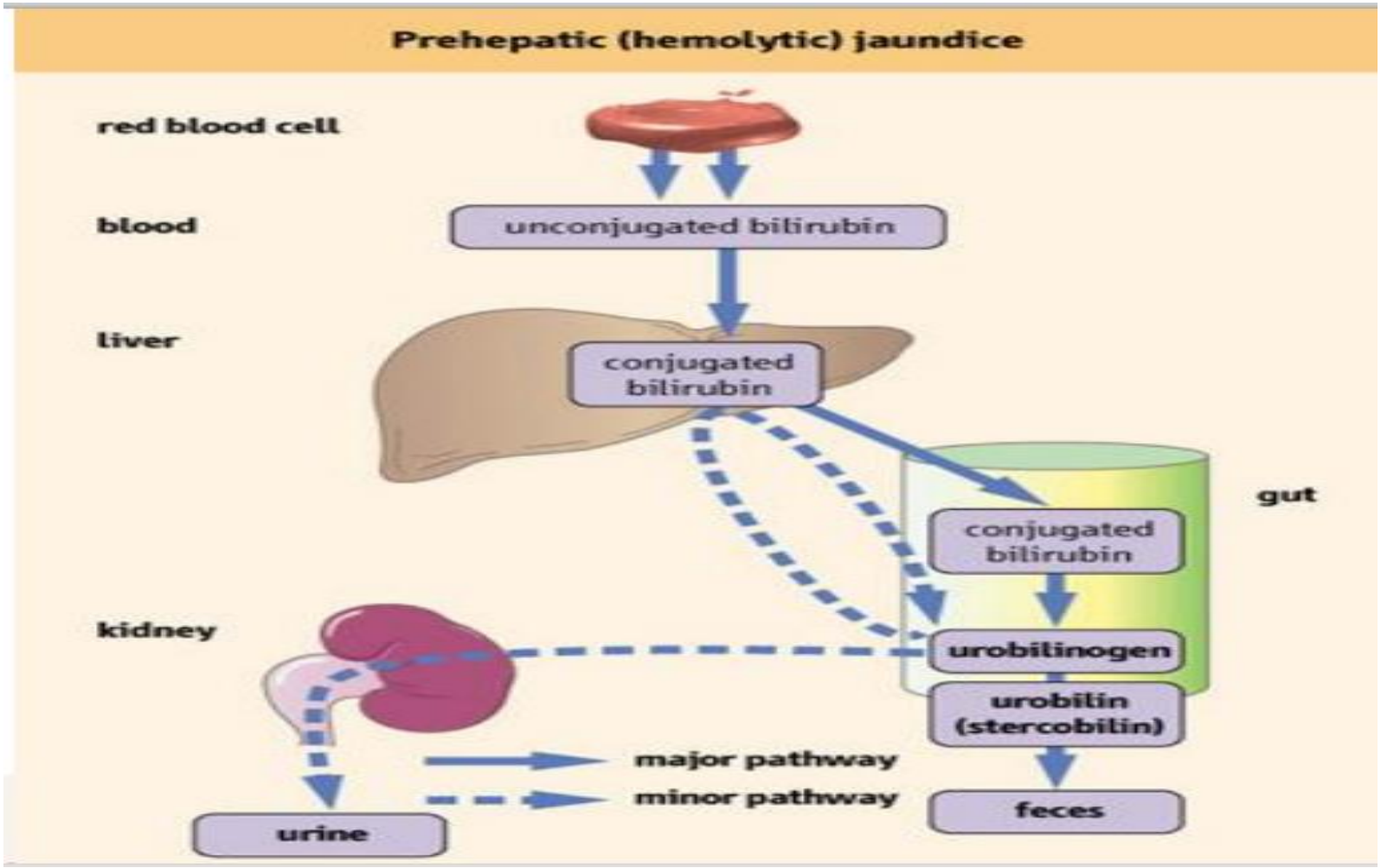
Prehepatic jaundice



Hepatic (hepatocellular) jaundice

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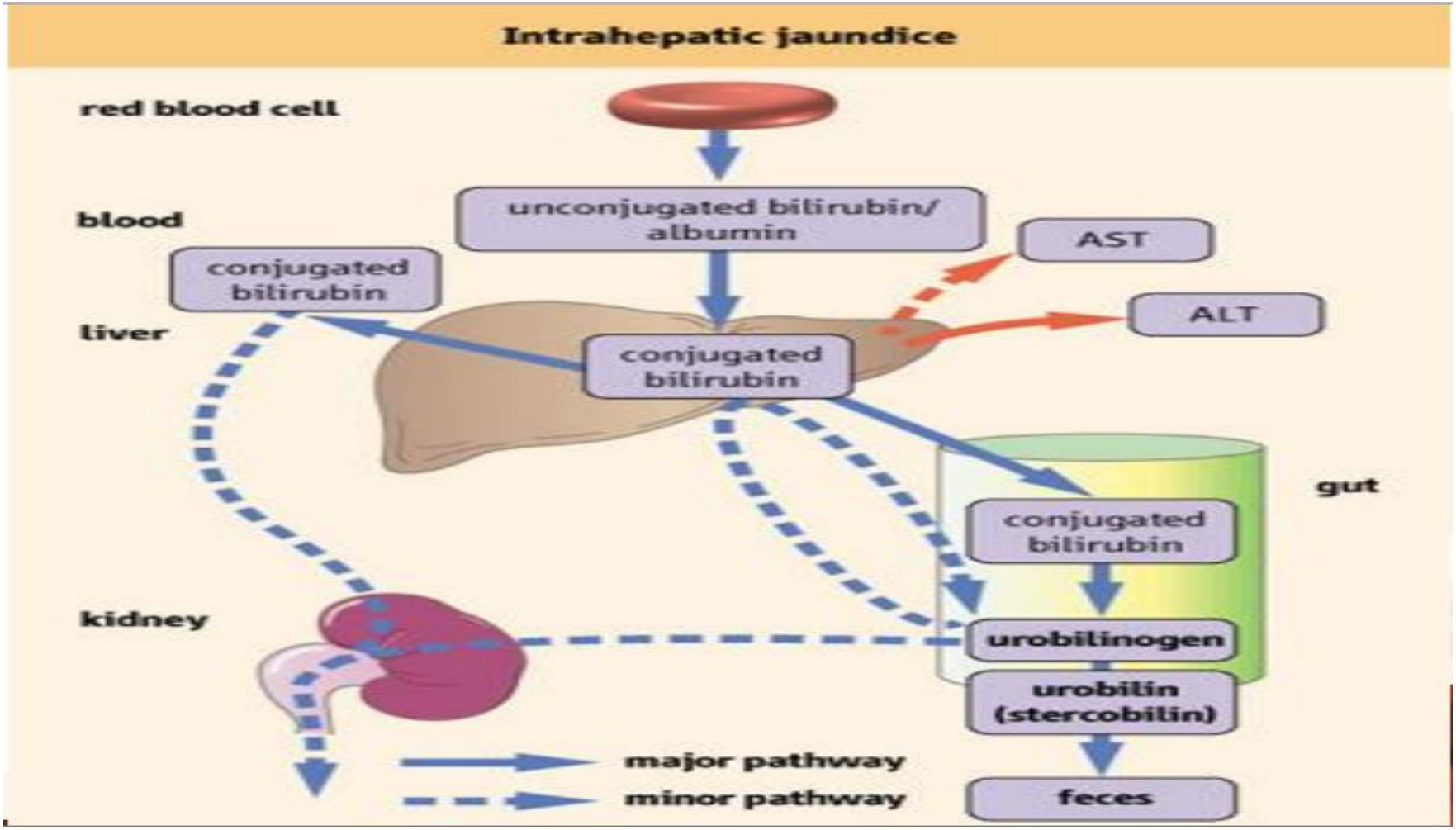
causes	Plasma bilirubin	Urine bilirubin	Van der Bergh reaction	Stools color
Hyperbilirubinemia may be due to: 1- Impaired uptake of bilirubin into hepatic cells. 2- Disturbed intra cellular protein binding or conjugation. 3- Disturbed active secretion of bilirubin into bile canliculi. ♦ The causes may be due to: * **Damage of liver cells** e.g., viral hepatitis, drugs, chemical, alcohol, or toxins. ***Autoimmune** hepatitis. * **Genetic errors** in **bilirubin metabolism.** * **Genetic errors in specific proteins**.	The diseased liver cells are unable to take all the unconjugated hemobilirubin formed, increasing its concentration in the blood. Also, there is intrahepatic biliary duct obstruction that leads to regurgitation of conjugated bilirubin to blood. ♦ Both types of bilirubin (conjugated & unconjugated) are present in blood in high concentration.	Urine appears dark brown due to filtration of excess conjugated bilirubin through the kidney.	biphasic	Stools appear pale grayish in color due to deficiency of stercobilin.

Hepatic (hepatocellular) jaundice

•In this case, hyper-bilirubinemia is usually accompanied by other abnormalities in biochemical markers of liver function such as: Alanine amine transferase (ALT, SGPT), Aspartate amine transferase (AST, SGOT), alkaline phosphatase (ALP) and Gamma-glutamyltransferase (GGT).

•By looking at the ration between these different liver enzymes, we can distinguish the causes of jaundice whether it is from biliary (cholestatic) or liver (hepatic). The main diagnostic tip is in the biliary obstruction, the ALT goes up and down (pulsatile increase) and the bilirubin concentration in the blood is high. But in hepatic jaundice, ALT shows persistent increase for along period of time (months).

Hepatic (hepatocellular) jaundice



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Posthepatic (obstructive) jaundice

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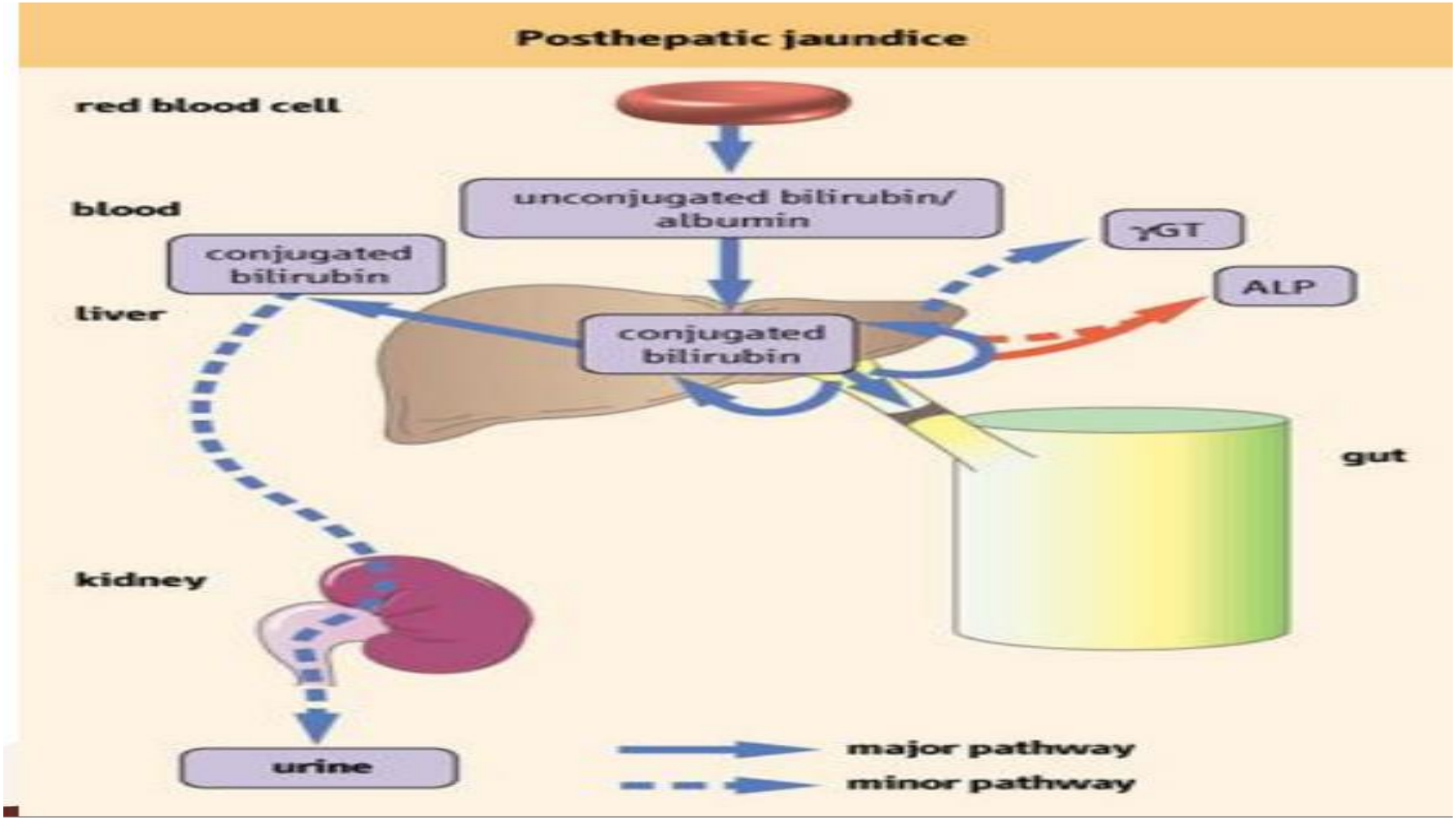
causes	Plasma bilirubin	Urine bilirubin	Van der Bergh reaction	Stools color
Caused by an obstruction of the biliary tree: 1- **Intrahepatic bile duct obstruction** e.g * Drugs * Primary biliary cirrhosis * Cholangitis. **2- Extrahepatic bile duct obstruction** e.g * Gall stones. * Cancer head pancreas. * Cholangiocarcinoma.	The rate of bilirubin formation is normal, bilirubin enters the liver cells and become conjugated in the usual way. The conjugated bilirubin formed simply cannot pass into small intestine and it returns back into blood.	conjugated bilirubin is filtered through the kidney and appears in urine giving it dark brown (liquorice) color. Urine is free from urobilinogen.	direct.	Stools are clay color due to absence of Stercobilin.

Posthepatic (obstructive) jaundice



The Doctor said this slide just for reading ☺

The causes of jaundice

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

Neonatal Jaundice:

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- Common, particularly in premature infants .
- Transient (resolves in the first 10 days)
- Due to immaturity of the enzymes involved in bilirubin conjugation
- Due to its hydrophobicity(unconjugated bilirubin) 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 (conjugated bilirubin) non-toxic form.
- If necessary, exchange blood transfusion is used to remove excess bilirubin.
- Phenobarbital (drug) can be administered to the mother prior to an induced labor of a premature infant – crosses the placenta and induces the synthesis of UDP glucuronyl transferase.
- Jaundice within the first 24 hrs of life or which takes longer then 10 days to resolve is usually pathological, needs to be investigated.

Neonatal Jaundice:

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Liver Secretion of Cholesterol and Gallstone Formation

- Under abnormal conditions, the cholesterol may precipitate in the gallbladder, resulting in the formation of *cholesterol gallstones*. The amount of cholesterol in the bile is determined partly by the quantity of fat that the person eats, because liver cells synthesize cholesterol as one of the products of fat metabolism in the body. For this reason, people on a high-fat diet over a period of years are prone to the development of gallstones.
- Inflammation of the gallbladder epithelium, often resulting from low-grade chronic infection, may also change the absorptive characteristics of the gallbladder mucosa, sometimes allowing excessive absorption of water and bile salts but leaving behind the cholesterol in the bladder, and then progressing to large gallstones.

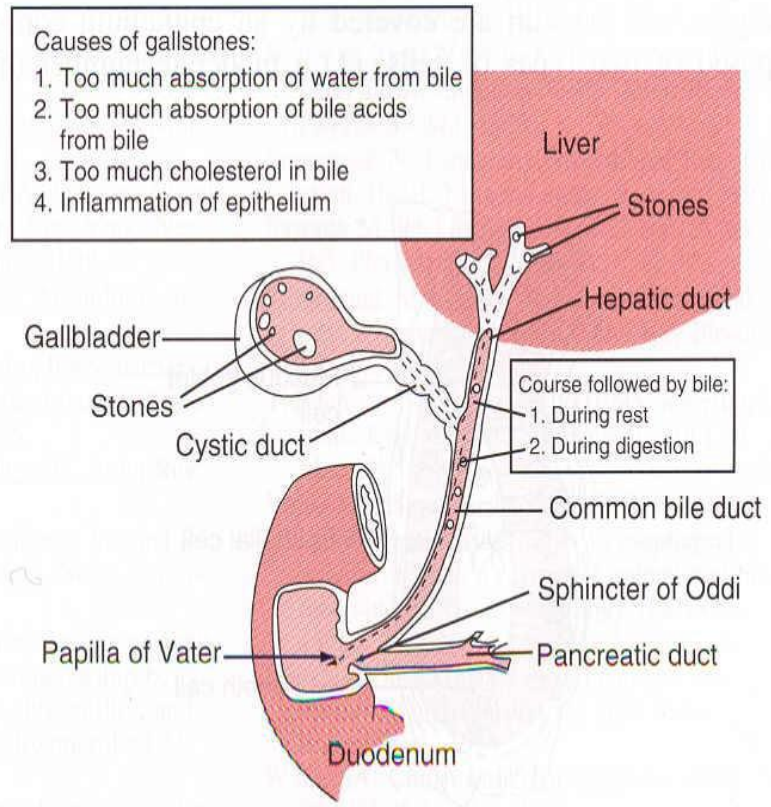

FIGURE 64-12

Formation of gallstones.

- ***Mechanisms of hyperbilirubinemia:***

Hyperbilirubinemia may involve predominantly unconjugated or conjugated bilirubin.

- **Unconjugated hyperbilirubinemia** is most often caused by ≥ 1 of the following:
  - Increased production (excessive breakdown of RBCs)
  - Decreased hepatic uptake
  - Decreased conjugation
- **Conjugated hyperbilirubinemia** is most often caused by ≥ 1 of the following:
  - Dysfunction of hepatocytes (hepatocellular dysfunction)
  - Slowing of bile egress from the liver (intrahepatic cholestasis)
  - Obstruction of extrahepatic bile flow (extrahepatic cholestasis)

We recommend you to see this video *music* ☺

http://www.youtube.com/watch?v=LH-ptH2ifvw

	prehepatic Hemolytic)(	Hepatic (hepatocellular)	Posthepatic (obstructive)
Unconjugated	↑	↑	Normal
Conjugated	Normal	↑	↑
VDB	Indirect	Biphasic	Direct
AST & ALT	Normal	↑	Normal
ALP & yGT	Normal	Normal	↑
Urine bilirubin	Absent	Present (dark brown)	Present (liquorice)
Urine urobilinogen	Present	Present	Absent
Stole stercobilin	Darker ↑	Pale grayish ↓	Absent (Clay Color)

VDB = Van Den Bergh Rection ALT= Alanine amine transferase liquorice= very dark

AST = Aspartate amine transferase yGT= y glutamyl transpeptidase

QUESTIONS

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1-Bilirubin is a waste product released during the break down of:

a) Mast cells
b) Red blood cells
c) White blood cells
d) Platelets

2- Jaundice is also known as:

a) Icterus
b) Hemophilia
c) Anemia
d) Hypercholesterolemia

3-Hemolytic jaundice occurs due to:

a) Liver diseases
b) Rapid destruction of erythrocytes or red blood cells
c) Intestinal diseases

B
A
B

3- Obstruction of bile duct causes jaundice.

a) True

b) False

4- Jaundice caused due to obstruction of bile duct is also referred to as:

a) Hemolytic jaundice

b) Hepatocellular jaundice

c) Cholestasis

5- Blood incompatibility between the mother and baby can cause jaundice in the new born:

a) True

b) False

6- Full term babies have a lower risk of contracting jaundice than the premature babies:

a) True

b) False

A
C
A
A

1. Increased levels of serum bilirubin is known as:

A. Sprue.
B. jaundice
C. cholestasis

2. One of the causes of jaundice is:

a) Hypotension
b) Increase fatty food intake c) Liver cirrhosis
d) Inflammatory bowel disease.

B

3. Which one of the following feature is commonly seen in cases of carcinoma of the head of pancreas?

A. obstructive jaundice
B. thrombosis of mesenteric artery
C. heamolytic anemia

C

4. Van der Bergh reaction in posthepatic jaundice is :

A. Biphasic
B. Direct
C. Indirect

A

B

5. Obstructive jaundice:

a) Results from excessive destruction of the RBCs.
b) Involves excretion of urine having a normal color.
c) Involves excretion of stools darker than normal.
d) Causes excess fat loss in the stools.

6- In hepatic jaundice: D

a) Both haemobilirubin & cholebilirubin blood levels are decreased. B
b) The liver functions are depressed & the plasma albumin level is decreased. A
c) The urine colour is normal while that of the stools is darker than normal.
d) Fat digestion & absorption are not affected.

7. Jaundice can be diagnosed by:

a) Blood tests
b) ECG
c) EEG

THE END

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If there are any Problems or Suggestions,
Feel free to contact us:

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THANK YOU

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Actions Speak Louder Than Words