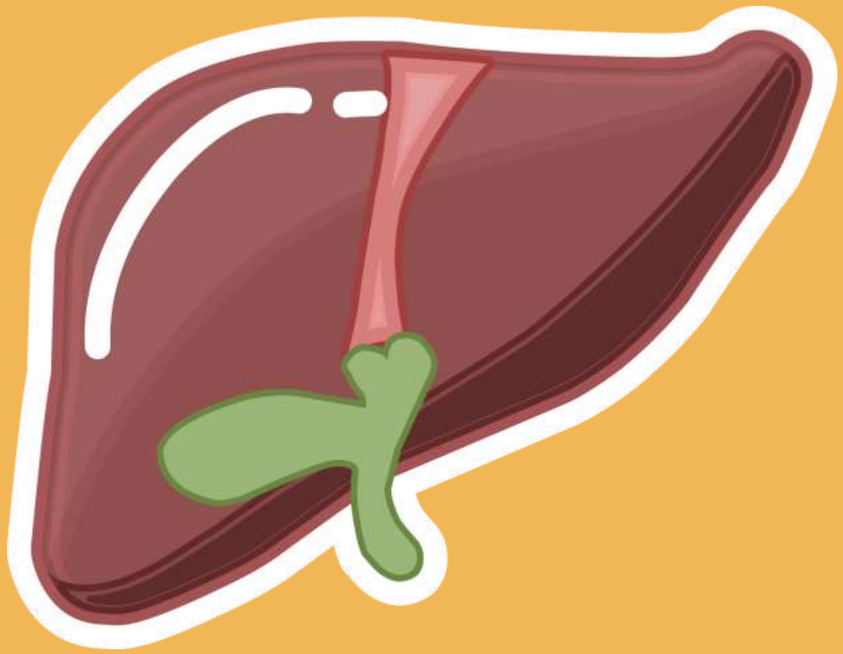
APPROACH TO PATIENT WITH JAUNDICE



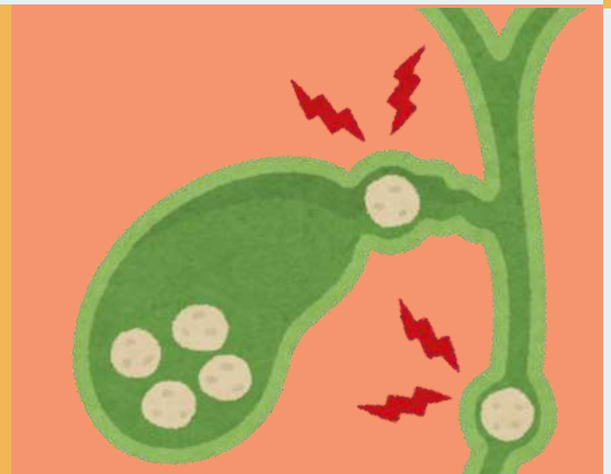
Supervised by: Dr. Ahmad Atia

Done by:

Nizar Almaaitah

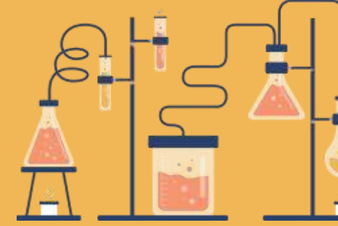
Mohmmad Alkiswani

Hamzeh Al-Tamimi



Internal Medicine

Jaundice



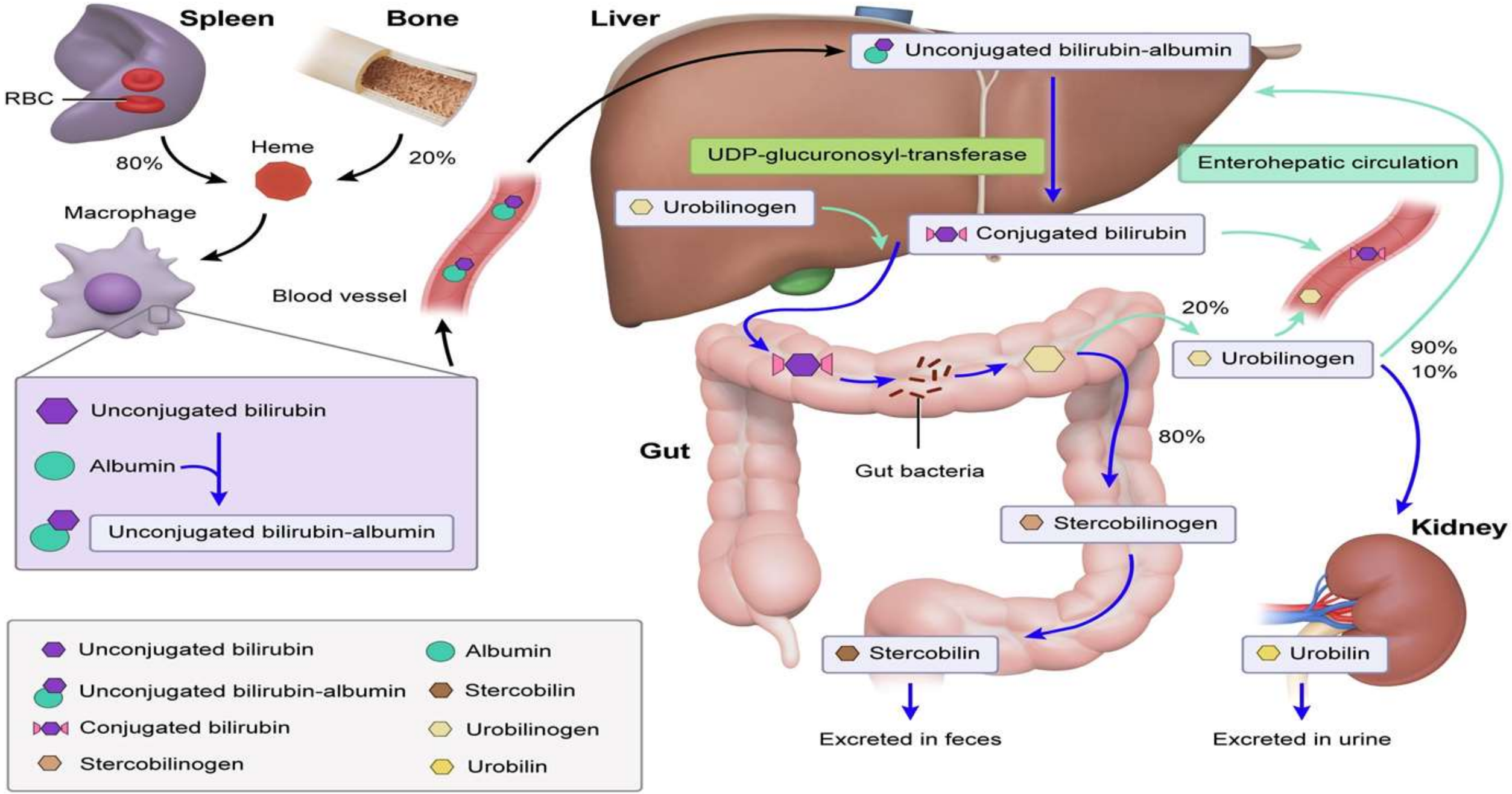
- **Yellow coloration of skin, mucous membranes, and sclera due to overproduction or under clearance of bilirubin (Hyperbilirubinemia)**

- Clinical jaundice usually becomes evident when total bilirubin is **>2 to 3 mg/dL**

- First site where bilirubin deposits is **sclera** due presence of high amount of Elastin protein which has high affinity for bilirubin !

Bilirubin Metabolism

Bilirubin Metabolism Pathway



Bilirubin Metabolism.

- **Hemoglobin is converted to bilirubin in the spleen(unconjugated).**

- This **unconjugated** bilirubin circulates in plasma, bound to albumin. This bilirubin-albumin complex is **not water soluble**; therefore, it is not excreted in urine.

- In the **liver**, it dissociates from albumin, and the bilirubin is **conjugated** via liver enzymes and excreted into the intestine, where bacteria act on it to produce urobilinogen , urobilin and stercobilin .

- **UDP-glucuronosyltransferase** turns unconjugated bilirubin into conjugated bilirubin !

REMEMBER !

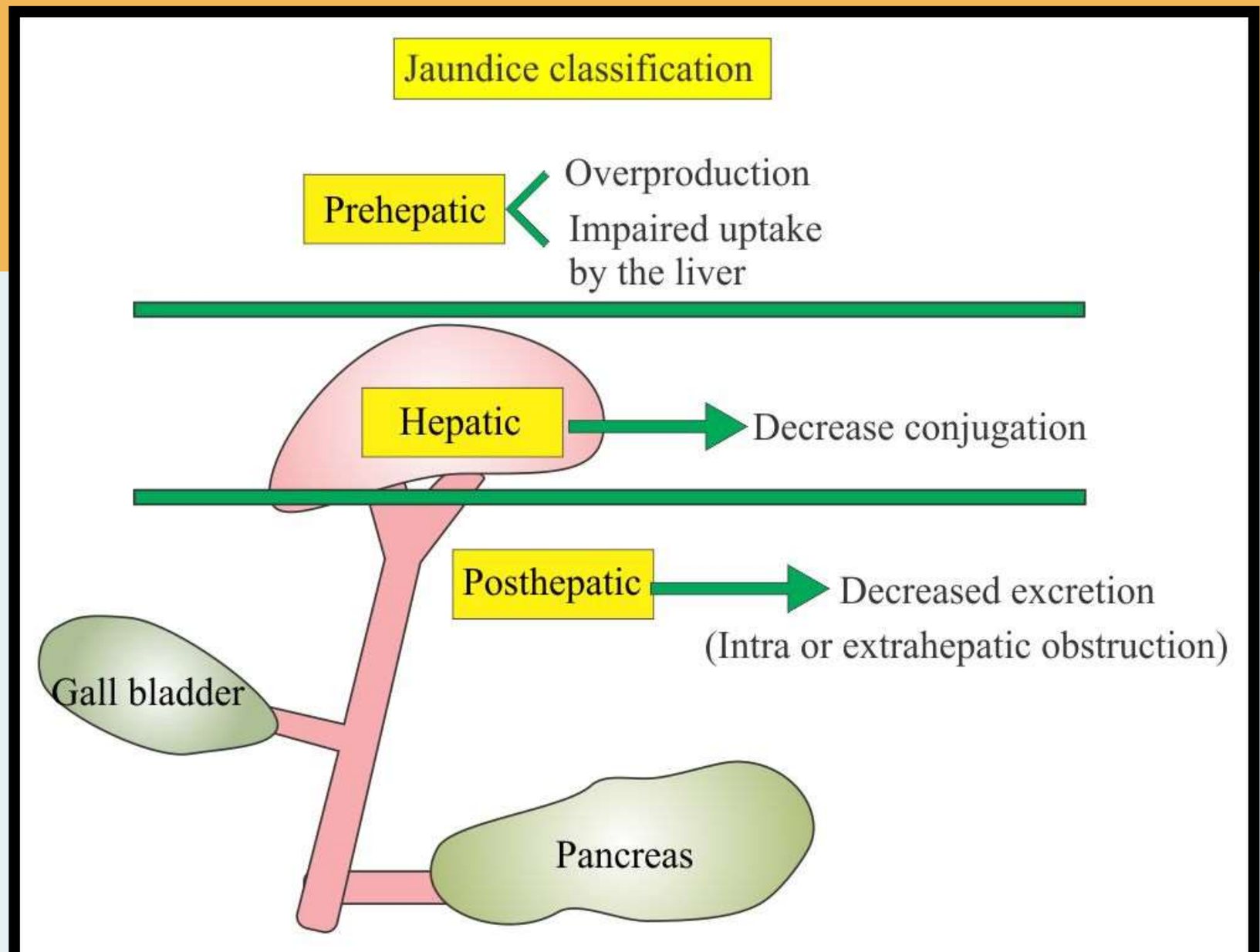
- Unconjugated bilirubin is not water soluble
  But Conjugated is water soluble!

- Stercobilin is excreted in Stool (brown color) ,
  Urobilin is excreted in Urine

TYPES OF JAUNDICE :

PRE HEPATIC	HEPATIC	POST HEPATIC
Excessive amount of bilirubin is presented to the liver due to excessive hemolysis	Impaired cellular uptake, defective conjugation or abnormal secretion of bilirubin by the liver cell	Impaired excretion due to mechanical obstruction to bile flow
Elevated unconjugated bilirubin in serum	Both conjugated and unconjugated bilirubin may be elevated in serum	Elevated conjugated bilirubin in serum

TYPES OF JAUNDICE :



▪ Prehepatic Jaundice

As bilirubin is unconjugated at this stage, this is called :
unconjugated hyperbilirubinaemia.
(The colour of stool & urine are Normal)

1-Hemolytic Anemia	Increased haemolytic activity increases U.C bilirubin. (hereditary spherocytosis ,sickle cell anaemia, thalassaemias ,G6PD deficiency, pyruvate kinase deficiency)
2-Crigler-Najjar syndrome	**type 1** : **complete** absence of UDP enzyme in the liver , cause severe UC hyperbilirubinemia . **type 2** : Reduced UDP activity , less severe

▪ Prehepatic Jaundice

As bilirubin is unconjugated at this stage, this is called :
unconjugated hyperbilirubinaemia.
(The colour of stool & urine are Normal)

3-Gillbert Syndrome

- most common hereditary cause of increased bilirubin.
- Reduced activity(70%-80%) of the UDP glucuronyl transferase, which conjugates bilirubin .
- Common cause of isolated elevation of unconjugated bilirubin.
- Exacerbated by stress (e.g., fasting, fever, alcohol, and infection)

▪ Hepatic Jaundice

- ✓ Due to Hepatocelluler disease that cause a reduction in **counjugation** and **secretion** of bilirubin
- ✓ **BOTH conjugated & unconjugated hyperbilirubinaemia. (pale stool & dark urine)**

causes :

- Hepatocytes can be **damaged** by **viruses**, **alcohol**, autoimmune processes or drugs and can result in permanent scarring, which, if left untreated, can progress to **cirrhosis**.

-Hepatocellular necrosis : **Hepatitis** , **Cirrhosis**, **Drug-related** (**paracetamol, methotrexate**)

- Infiltrative: TB
- Toxins -Hepaticcrisis in sickle cell disease

PostHepatic Jaundice (Obstructive)

- ✓ **Conjugated Hyperbilirubinemia**
- ✓ **Stool is pale & Urine is Dark**

Intrahepatic

- Blockage of Bile Canaliculi
  - Dubin-Johnson syndrome : (Mild autosomal resseccive disease characterized by mild impairement in **biliary secretion** of conjugated bilirubin)

-Rotor syndrome : (autosomal resseccive disease characterized by non-hemolytic jaundice due to chronic elevation of predominantly conjugated bilirubin)

- Infiltrative tumors

PostHepatic Jaundice (Obstructive)

- ✓ **Conjugated Hyperbilirubinemia**
- ✓ **Stool is pale & Urine is Dark**

extrahepatic

- - Obstructive of bile ducts by **tumors**, CBD or CHD **stone** and **Stenosis**
- -Acute and chronic pancreatitis
- - Parasitic infections as Ascaris lumbricoides and liver Flukes

- Plasma bilirubin is conjugated,and other biliary metabolites,such as bile acids accumulate in the plasma→will cause **skin itching**

6.6 Common causes of jaundice

Increased bilirubin production

- Haemolysis (unconjugated hyperbilirubinaemia)

Impaired bilirubin excretion

- Congenital:
  - Gilbert's syndrome (unconjugated)
- Hepatocellular:
  - Viral hepatitis
  - Cirrhosis
  - Drugs
  - Autoimmune hepatitis
- Intrahepatic cholestasis:
  - Drugs
  - Primary biliary cirrhosis
- Extrahepatic cholestasis:
  - Gallstones
  - Cancer: pancreas, cholangiocarcinoma

Hypercarotonemia

- Hypercarotenaemia occurs due to excessive ingestion of carotene containing vegetables or in situations of impaired metabolism such as hypothyroidism

- A yellowish discoloration is seen on the face,palms and soles but not the sclera or conjunctiva,and this distinguishes it from jaundice

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 (as it lipid soluble)

- 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 .

- If necessary,exchange blood transfusion is used to remove excess bilirubin

- Phenobarbital is often times administered to Mom prior to an induced labor of a premature infant : crosses the placenta and induces the synthesis of UDP glucuronyltransferase

-Jaundice within the first 24 hrs of life or which takes longer then 10 days to resolve is usually pathological and needs to be further investigated .

Treatment options in infants

If a baby has moderate or severe jaundice, the following treatment options are required

1

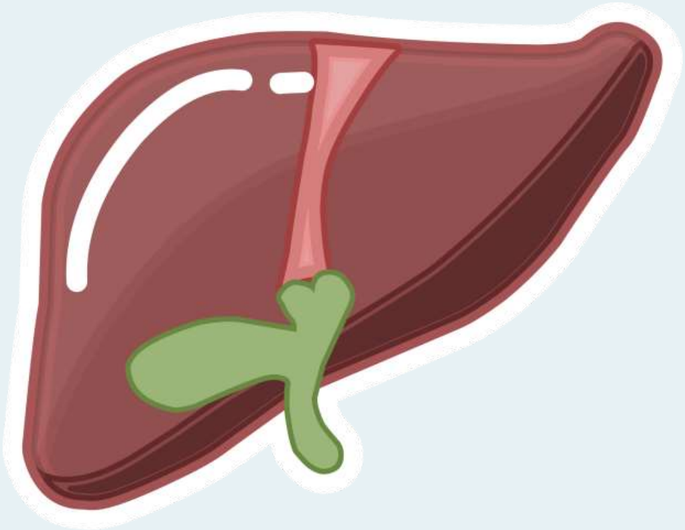
Phototherapy

2

Exchange Transfusion

when not respond to earlier treatments, the baby may require this procedures Here, small amounts of blood are repeatedly withdrawn and then replaced with donor blood.This process helps dilute bilirubin

- HISTORY
- PHYSICAL EXAMINATION
- LABS TEST
- IMAGING
- DDX



HISTORY:

ASK ABOUT:

Introduce yourself and take a verbal consent

Patient profile

Chief complaint

History of present illness

History of present illness

-When did the skin discoloration start? How did it start? (Onset)

Sudden (acute hepatitis, choledocholithiasis, cholangitis, or hemolysis) or gradual (Pancreatic or hepatobiliary cancer)

course (on and off, gradual, sudden)

- Site & distribuation .

- Duration .

HISTORY:

ASK ABOUT:

Associated symptoms

Have you noticed any changes in your stool and urine color?

Pale stool and dark urine (increased conjugated bilirubin) (obstructive jaundice, cholithiasis, or primary biliary cirrhosis),

normal stool and dark urine (increased conjugated and unconjugated bilirubin) (hepatic causes, hepatitis, or chemicals) or,

normal stool and urine color (increased unconjugated bilirubin) (pre-hepatic causes or hemolysis)

HISTORY:

ASK ABOUT:

Associated symptoms

Do you have any skin itching (pruritus)? (Cholestatic liver disease)

Do you have fever? (Cholangitis or acute hepatitis)

Do you have weight loss and loss of appetite? (Pancreatic or hepatobiliary cancer)

Change in appetite (fear of eating)

Do you have abdominal pain? (Acute hepatitis, choledocholithiasis, or cholangitis)

What Is the Implication of Painful Versus Painless Jaundice?
Painful jaundice implies an acute biliary obstruction, usually due to a gallstone, and is usually associated with inflamma-tion/infection, such as acute cholangitis. Painless jaundice suggests a more insidious obstruction as seen with malignancy or autoimmune diseases of the biliary system.

HISTORY:

ASK ABOUT:

Past medical and surgical history

Have you had any previous similar symptoms?

Have you ever had a blood transfusion? (Hepatitis B or C)

Have you been immunized against hepatitis B?

Have you been diagnosed with IBD? (Primary sclerosing cholangitis)

Have you been diagnosed with sickle cell disease? (Hemolysis)

Waxing and Waning of jaundice suggestive of CBD stone and periampullary carcinoma .

Have you had any recent contact with patients with jaundice or liver problems? (Hepatitis A)

Have you had any surgeries (e.g., pancreatic or biliary)?

HISTORY:

ASK ABOUT:

Jaundice: hepatitis	Paracetamol (overdose) Pyrazinamide Rifampicin Isoniazid
Jaundice: cholestatic	Flucloxacillin Chlorpromazine Co-amoxiclav

Medication history

Do you take any medication or use herbals?

Drug-induced hepatotoxicity (e.g., Paracetamol (overdose) , amoxicillin, or isoniazid)

Family history

Do you have a family history of similar symptoms or any liver diseases?

(Hemochromatosis,Wilson's disease, Gilbert syndrome, or Crigler-Najjar syndrome)

HISTORY:

ASK ABOUT:

Social history

Have you ever used any intravenous drugs or had tattoos? (Hepatitis B or C)
Do you drink alcohol? (Liver cirrhosis)
-ask about Smoking

Have you traveled recently? If yes, please indicate the place? (To endemic area of hepatitis A)
What is your occupation? (Possible contact with hepatotoxins)

also ask Systemic review

PHYSICAL EXAMINATION :

Vital signs : BP , Temperature , RR , HR

WHAT TO EXAM	FINDINGS
EYES	Jaundice under the sclera of eyes and,pallor
HANDS	Clubbing , palmar erythema , duputryen's contracture .
CHEST	Spider angioma , gynecomastia in male , spider telangiectasias .
ABDOMEN	HEPATOMEGALY , ASCITES , DISTENDED ABDOMINAL VEIN , CAPUT medusa , hair distribution. DO FULL ABDOMINAL EXAMINATION
LOWER LIMB	EDEMA , VARICES .
Genitalia	Testicular atrophy.

PERIPHERAL EXAM:

Hands

Symmetrically cold (Hypovolemia)

Muscle wasting (Alcoholic liver disease)

Flapping tremor (Hepatic encephalopathy)

Nails

Clubbing (Chronic liver disease or IBD)

Capillary refill (Hypovolemia if >2 s)

Leukonychia (Hypoalbuminemia)

Koilonychias (Iron deficiency anemia)

PERIPHERAL EXAM:

If the examiner asks you to do focus in abdominal examination, skip the peripheral examination.

Fingers

Nicotine staining (Smoking)

Palm

Pallor (Anemia)

Palmar erythema (Chronic liver disease)

Dupuytrn's contracture (Alcoholic liver disease)

Palmar xanthomata (Hyperlipidemia)

Dorsum

Tendon xanthomata (Hyperlipidemia)

Usually muscle wasting is noted in interosseous, thenar,& hypothenar muscles

PERIPHERAL EXAM:

Arm and axilla

Bruising (Increased prothrombin time due to liver failure)

Petechiae (Thrombocytopenia)

Scratch marks (Chronic cholecystitis)

Eyes

Pallor in conjunctiva (Anemia)

Jaundice in sclera (Pre-hepatic, hepatic, or post-Hepatic)

Xanthelasma (Hyperlipidemia)

Iritis (IBD)

Kayser Fleischer ring (Wilson disease)

PERIPHERAL EXAM:

Mouth

Candidiasis (Iron deficiency or immunodeficiency)

Glossitis (Iron/B12/folate deficiency)

Aphthous ulcer (chron's disease or celiac disease)

Fetor hepaticus (Severe liver disease)

Angular stomatitis (Iron/B12/folate deficiency)

Salivary glands

Parotid enlargement (Alcoholic liver disease)

Fetor hepaticus is sweet smell of breath

PERIPHERAL EXAM:

Chest

Spider nevi (chronic liver disease)

Gynecomastia (chronic liver disease)

Left-side supraclavicular lymph node (Virchow's node) (Gastric cancer)

Lower limb

Edema (Liver disease)

Clubbing of the toes (chronic liver disease or IBD)

LABORATORY TESTS :

1. CBC: Hb , MCV , RDW , reticulocyte count
2. Liver function test .(LFT)

-ALK-P (biliary tree injury – obstructive jaundice),

-GGT (more specific),

3. Metabolic panel .
4. Hepatitis Marker *..
5. INR,PT,PTT.
6. Albumin level .
7. Total serum bilirubin , direct and indirect bilirubin
8. Urine and stool analysis .
9. Special test according to suspected cause.

If unconjugated hyperbilirubinemia : CBC, reticulocyte count , haptoglobin LDH and peripheral smear may aid , in diagnosis of hemolysis as a cause of jaundice.

If conjugated hyperbilirubinemia: LFTs may point to the cause.

6.7 Urine and stool analysis in jaundice

	Urine			Stools
	Colour	Bilirubin	Urobilinogen	Colour
Unconjugated	Normal	–	++++	Normal
Hepatocellular	Dark	++	++	Normal
Obstructive	Dark	++++	–	Pale

IMAGING:

1. US or CT scan to assess biliary tract for obstruction or anatomical changes .
2. Additional tests : ERCP , MRCP , PTC .
3. Liver biopsy may be indicated in some cases to determine cause of hepatocellular injury

TREATMENT :

Treat the underlying cause .

DDX :-

Pre-hepatic cause (hemolytic disease)

Hepatic cause (hepatitis, crigler-najjar, dobin-jonson, liver mets, cirrhosis)

Post hepatic cause:

1- Luminal

a. CBD stone

b. Parasitic disease (Ascaris, pinworms)

c. Hydatid cyst rupture (daughter cysts)

2- Mural

a. Stenosis (iatrogenic trauma)

b. Cholangicarcinoma

c. Primary sclerosing cholangitis

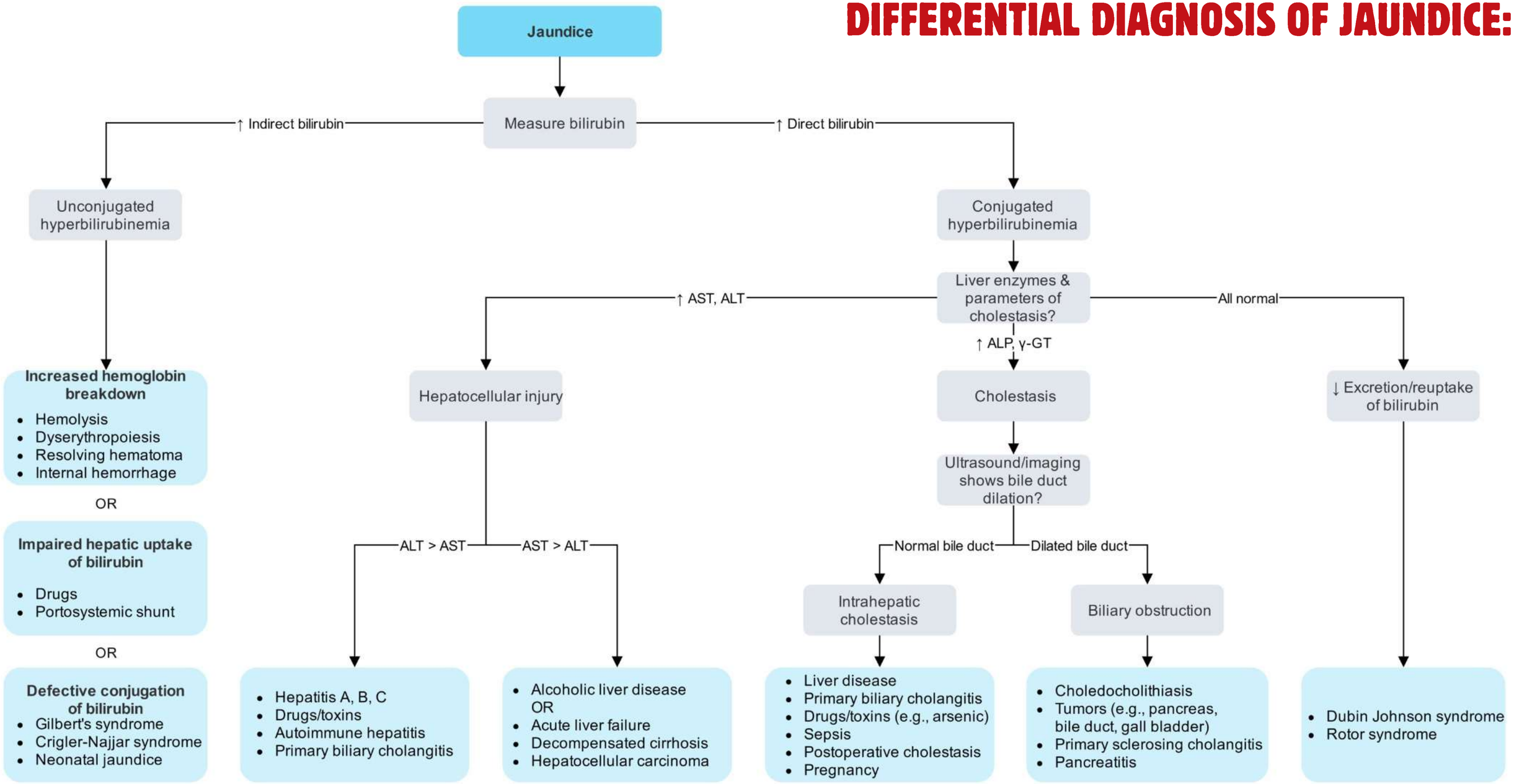
3- Extra-mural

a. Merrizi syndrome

b. Head of pancreas tumor

c. Klaskin tumor

DIFFERENTIAL DIAGNOSIS OF JAUNDICE:

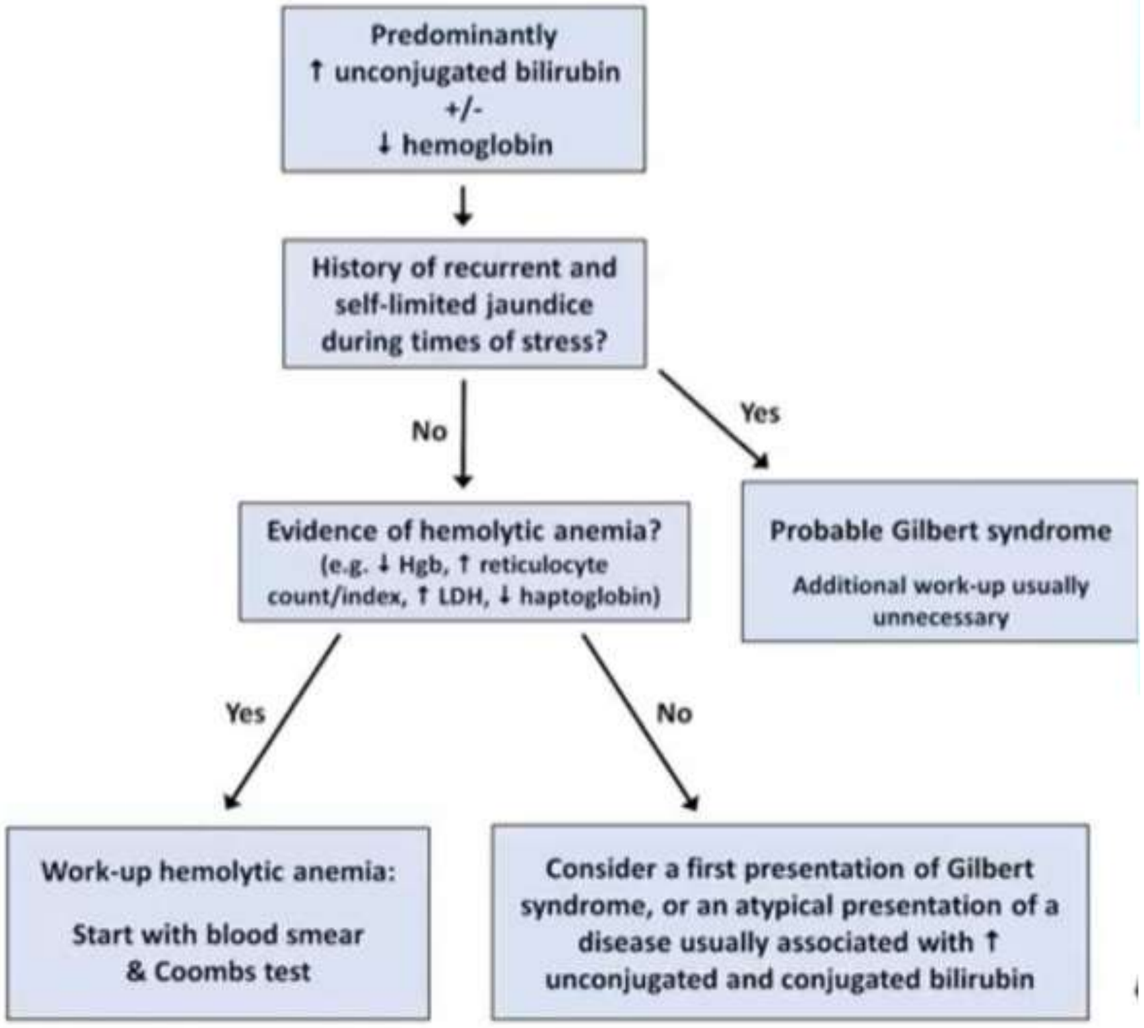


Amboss

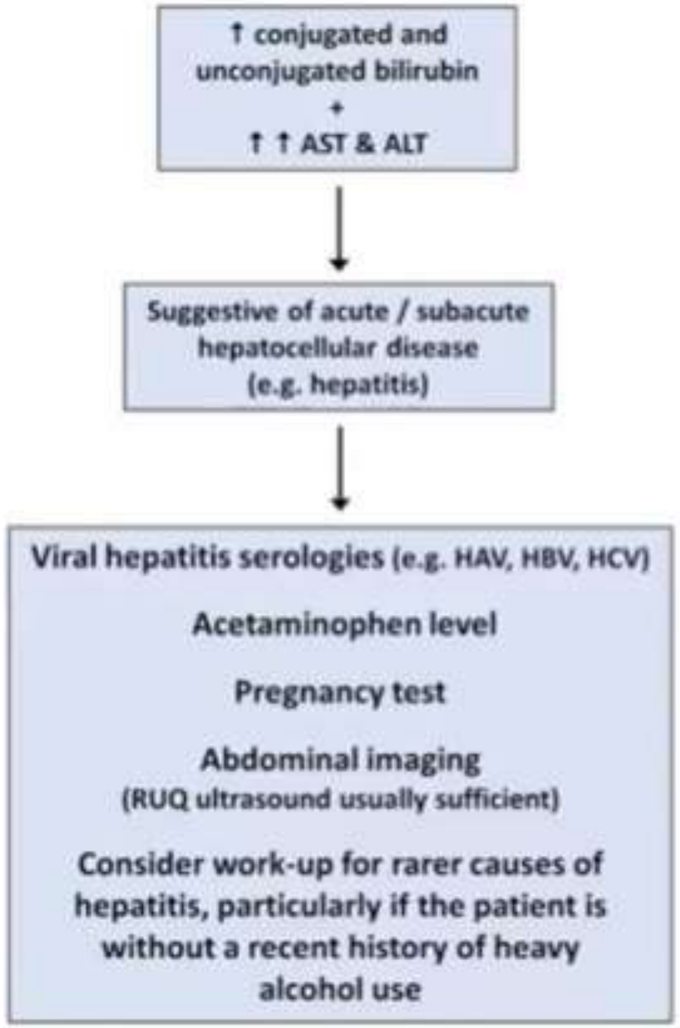
Overview of laboratory studies for jaundice [6]				
		Prehepatic jaundice	**Intrahepatic jaundice**	**Extrahepatic jaundice**
Indirect bilirubin		• ↑↑	• ↑	• Normal
Direct bilirubin		• Normal	• ↑	• ↑↑
Transaminases (AST, ALT)		• Normal	• ↑	• Normal
Cholestatic enzymes (ALP, GGT)		• Normal	• ↑	• ↑↑
Urinalysis	**Urine color**	• Normal • Dark urine in hemoglobinuria	• Dark urine	• Very dark urine
	Urinary bilirubin	• Normal	• ↑	• ↑↑
	Urinary urobilinogen	• ↑↑	• Normal or ↑	• ↓ [9]
Stool color		• Dark	• Variable: dark, pale, clay-colored	• Pale, clay-colored

DIFFERENTIAL DIAGNOSIS OF JAUNDICE:

First scenario



Second scenario



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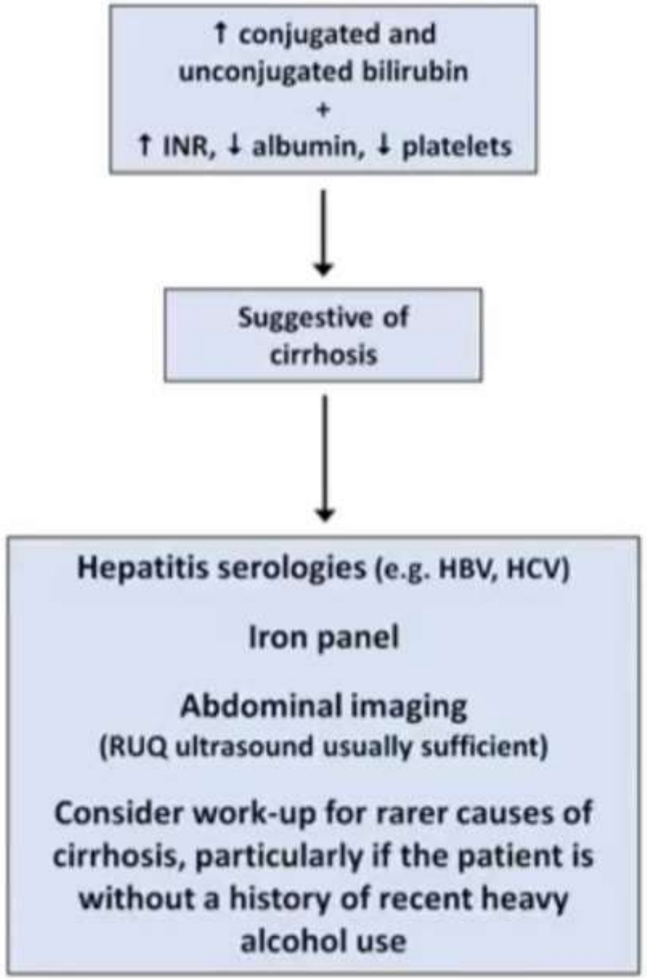
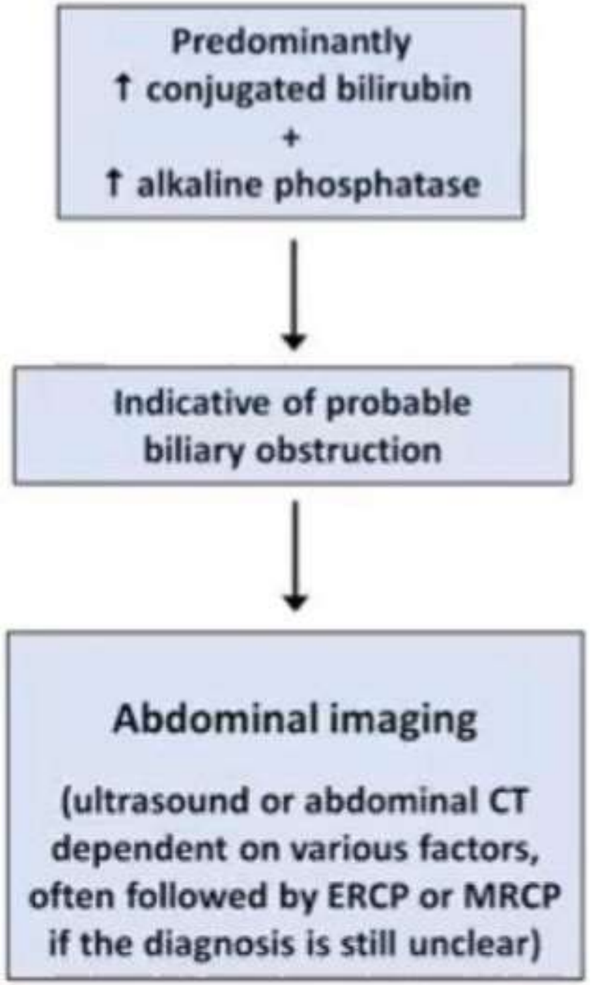
DIFFERENTIAL DIAGNOSIS OF JAUNDICE:

Third scenario



Fourth scenario



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