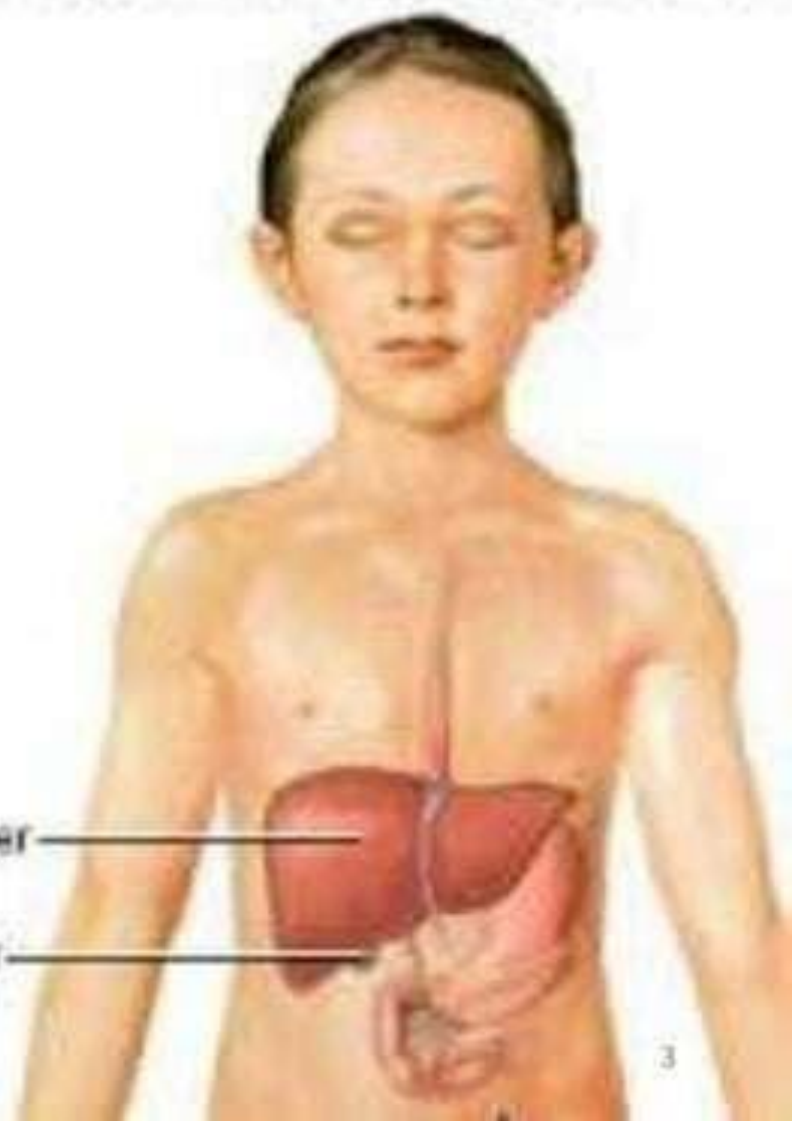
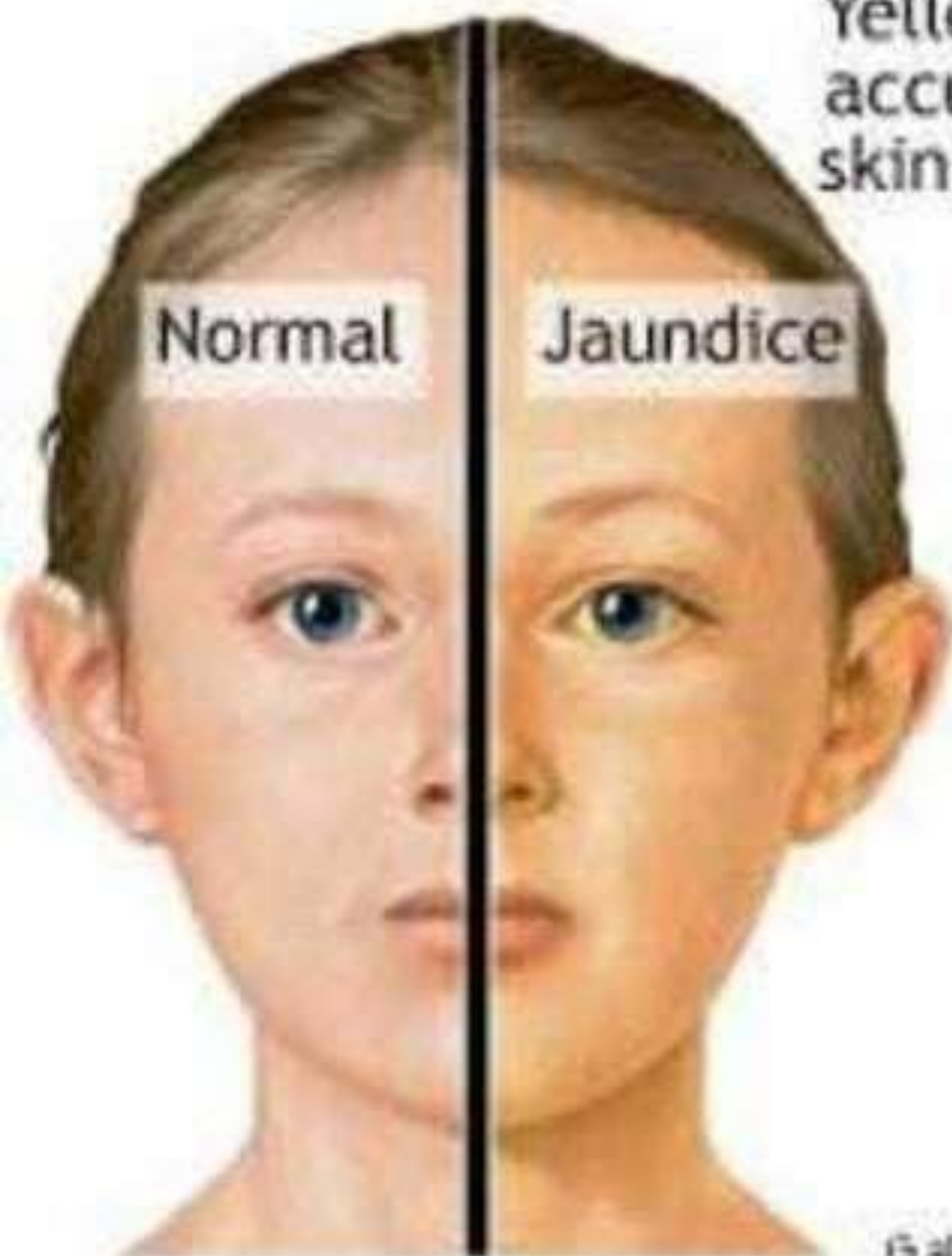


JAUNDICE

DEFINITION

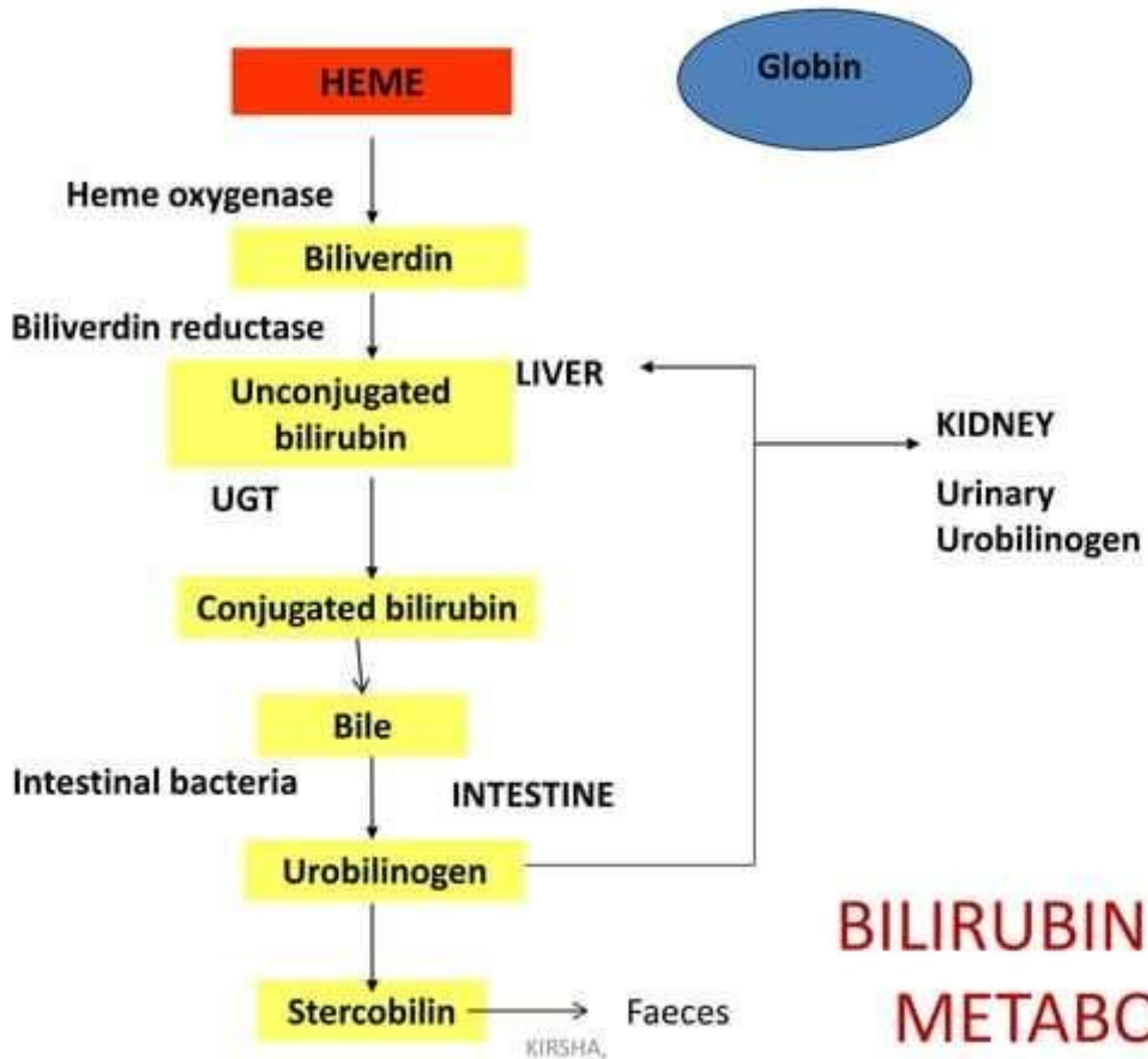
- Jaundice is yellowish discoloration of the skin, sclera and mucous membranes due to hyperbilirubinemia and deposition of bile pigments .
- It is usually detectable clinically, when the plasma bilirubin exceeds $50\mu\text{mol/L}$ ($\approx 3\text{mg/dL}$)
- Jaundice is not a disease, but rather a sign that can occur in many different diseases.

Yellowing is associated with the accumulation of bilirubin in the skin, most often caused by liver and gallbladder disorders



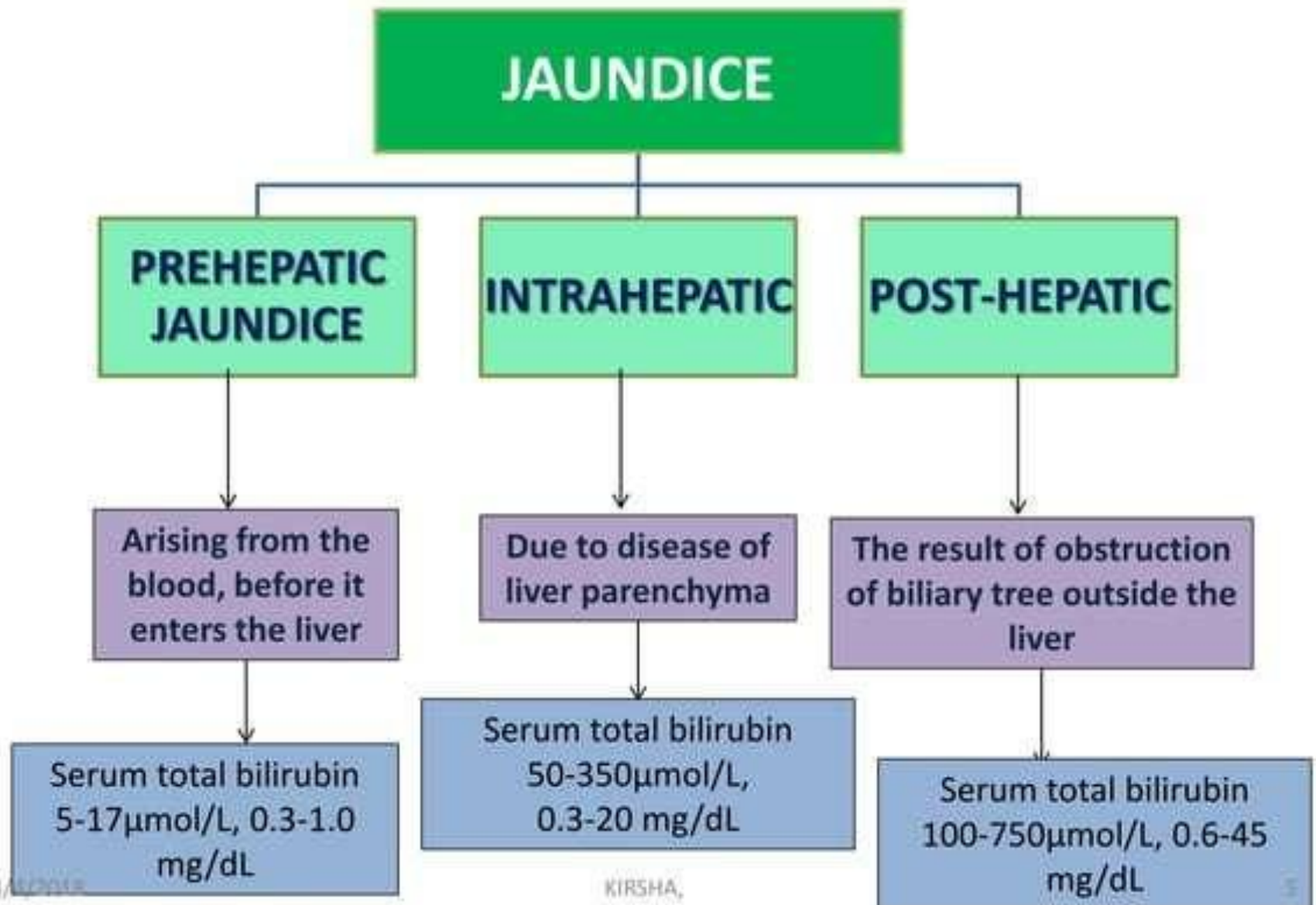
Liver

Gallbladder



BILIRUBIN METABOLISM

TYPES OF JAUNDICE



EPIDEMIOLOGY

- The prevalence of Jaundice varies with age and sex; newborns and older adults are most often affected.
- Approximately 20 percent of newborns develop Jaundice in the first week of life, primarily because of immaturity of the hepatic conjugation process.
- Congenital abnormalities, hemolytic or bilirubin uptake disorders, and conjugation defects are also responsible for Jaundice in infancy or childhood.
- Viral Hepatitis A is the most frequent cause of Jaundice among school-age children. Common duct stones, Alcoholic Liver Disease and Neoplastic Jaundice occur in middle-aged and older patients.

AETIOLOGY

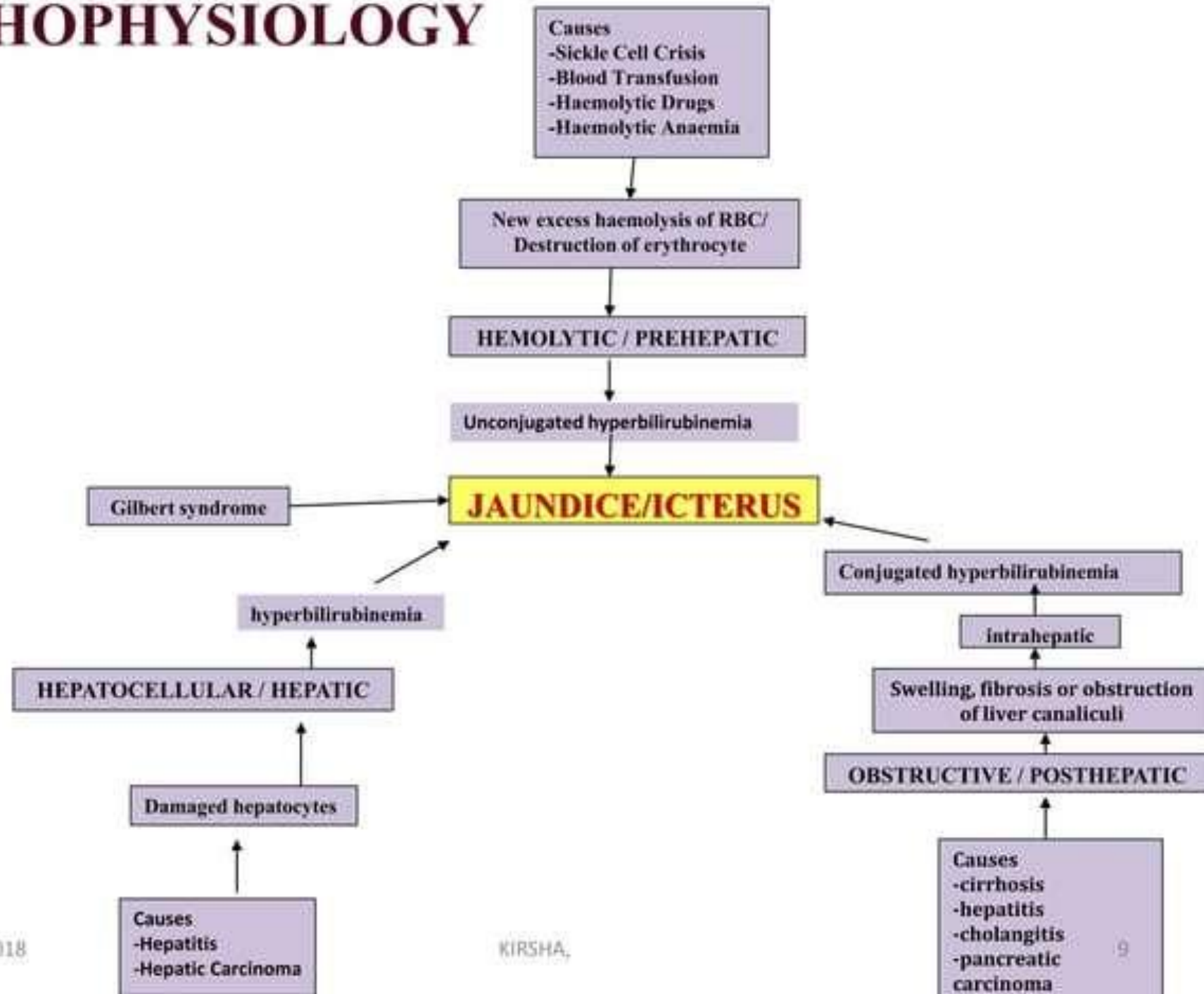
SITE OF ORIGIN	MECHANISM	CAUSES
Prehepatic	Increased heme liberation	<ul style="list-style-type: none"> • Hemolytic Anemia • Malaria • Reduced red cell lifespan
Intrahepatic	Defective liver metabolism	<ul style="list-style-type: none"> • Congenital enzyme defects • Iron storage disease • Reduced hepatic bilirubin uptake
	Obstruction of small bile ducts	<ul style="list-style-type: none"> • Alcoholic Cirrhosis • Autoimmune Liver Disease • Drugs and environmental chemicals • Hepatic Tumors • Pregnancy • Viral or other infections • Gall Stones • Primary Biliary Cirrhosis

Post-hepatic	Obstruction of large bile ducts	<ul style="list-style-type: none"> • Infection or inflammation of the biliary tree • Gall stones • Carcinoma of pancreas, gall bladder, bile ducts • Pancreatitis • Drugs
--------------	---------------------------------	--

DRUGS CAUSING JAUNDICE

ACTION	EXAMPLES	
Dose-dependent Hepatocellular Damage	Acetaminophen Salicylates	High Dose Tetracyclines
Dose-independent Hepatocellular Damage	Desulfuran, Isoflurane, Sevoflurane Dantrolene Ketoconazole	Antidepressants Aminosalicylic Acid Isoniacid Pyrizinamide, Ethambutol
Hemolysis	Methyl Dopa	Mefanamic Acid
Cholestasis	Carbimazole Oral Contraceptives Sodium Aurothiomalate Synthetic Anabolic Steroids	Chlorpromazine Chlorpropamide Erythromycin Estolate

PATHOPHYSIOLOGY



CAUSES OF JAUNDICE

Jaundice occurs when there is:

1. Too much bilirubin being produced from the liver and unable to remove from the blood (for example, patients with Hemolytic Anemia have an abnormally rapid rate of destruction of their red blood cells that releases large amounts of bilirubin into the blood)
2. A defect in the liver that prevents bilirubin from being removed from the blood, converted to bilirubin/glucuronic acid (conjugated) or secreted in bile.
3. Blockage of the bile ducts that decreases the flow of bile and bilirubin from the liver into the intestines. For example, the bile ducts can be blocked by Cancer, Gallstones, or inflammation of the bile ducts. The decreased conjugation, secretion, or flow of bile that can result in Jaundice is referred to as Cholestasis: however, Cholestasis does not always result in Jaundice.

Signs and Symptoms of Jaundice

Common signs and symptoms seen in individuals with Jaundice include:

- Yellow discoloration of
 1. The skin
 2. Mucous membranes
 3. The whites of the eyes
- Light-colored stools
- Dark-colored urine
- Itching of the skin.
- Nausea and vomiting
- Abdominal pain
- Fever
- Weakness
- Loss of appetite
- Headache
- Confusion
- Swelling of the legs and abdomen.

DIAGNOSIS

The yellowing of skin and eyes are likely to be the main clues a doctor will use before confirming a Jaundice diagnosis.

A physical examination will be carried out to look for signs of swelling of the liver and legs, ankles or feet which might indicate Cirrhosis of the liver.

- Hepatitis virus panel to look for infection of the liver
- Liver function tests
- Complete blood count to check for low blood count or Anemia
- Abdominal ultrasound
- Abdominal CT scan
- Endoscopic Retrograde Cholangio Pancreatography (ERCP)
- MRI Scan
- Liver biopsy

DIAGNOSTIC TESTS

FUNCTION TEST	PRE-HEPATIC JAUNDICE	HEPATIC JAUNDICE	POST-HEPATIC JAUNDICE
Total bilirubin	Normal / Increased	Increased	
Conjugated bilirubin	Normal	Increased	Increased
Unconjugated bilirubin	Normal / Increased	Increased	Normal
Urobilinogen	Normal / Increased	Increased	Decreased / Negative
Urine Color	Normal	Dark (urobilinogen + conjugated bilirubin)	Dark (conjugated bilirubin)
Stool Color	Normal	Normal/Pale	Pale
Alkaline phosphatase levels	Normal	Increased	
Alanine transferase and Aspartate transferase levels		Increased	
Conjugated Bilirubin in Urine	Not Present	Present	
Splenomegaly	Present	Present	Absent ¹³

PREVENTION OF JAUNDICE

Due to the wide range of potential causes, it's not possible to prevent all cases of Jaundice. However, there are four main precautions that you can take to minimize your risk of developing jaundice. They are:

1. Ensuring that you stick to the Recommended Daily Amount (RDA) for alcohol consumption
2. Maintaining a healthy weight for your height and build
3. If appropriate, ensuring that you're vaccinated against a Hepatitis A or B infection, vaccination would usually only be recommended depending on where in the world you're travelling .
4. Minimizing your risk of exposure to Hepatitis C because there's currently no vaccine for the condition .

GILBERT SYNDROME JAUNDICE

Gilbert's Syndrome is a harmless hereditary condition that results in mild Jaundice. During times of illness or stress, people with Gilbert's Syndrome will experience low levels of some bilirubin-processing enzymes in their livers, according to LabTestsOnline.com. Once diagnosed, Gilbert's Syndrome does not require further medical treatment.

DUBIN-JOHNSON SYNDROME

Autosomal disorder, due to deficiency in transporter protein MRP2 to transport conjugated bilirubin from hepatic cells to gall bladder. This leads to buildup of conjugated bilirubin in hepatic cells. Compensatory mechanism –upregulation of transport mechanism by MRP3 protein that bypasses conjugated bilirubin to blood- passes to kidneys producing even darker urine.

NEONATAL JAUNDICE

Jaundice is clinically detectable in the newborn when the serum bilirubin levels are greater than 85 $\mu\text{mol/L}$. This occurs in approximately 60% of term infants and 80% of preterm infants.

Neonatal Jaundice first becomes visible in the face and forehead. Blanching reveals the underlying colour. Jaundice then gradually becomes visible on the trunk and extremities.

SIGNS AND SYMPTOMS OF NEONATAL JAUNDICE

Newborns, as the bilirubin level rises, jaundice will typically progress from the head to the trunk, and then to the hands and feet. Additional signs and symptoms that may be seen in the newborn include:

1. Poor Feeding
2. Lethargy
3. Changes In Muscle Tone
4. High-pitched Crying
5. Seizures.

JAUNDICE IN PREGNANCY

CHOLESTASIS OF PREGNANCY

Cholestasis of pregnancy is an uncommon condition that occurs in pregnant women during the third trimester. The Cholestasis often is accompanied by itching but infrequently causes Jaundice. There also is an association between Cholestasis of pregnancy and Cholestasis caused by oral Estrogens, and it has been hypothesized that it is the increased estrogens during pregnancy that are responsible for the Cholestasis of pregnancy

ACUTE FATTY LIVER OF PREGNANCY (AFLP)

It is a very serious complication of pregnancy. It occurs late in pregnancy and results in failure of the liver. It can almost always be reversed by immediate delivery of the fetus. There is an increased risk of infant death. Jaundice is common, but is not always present in AFLP.

PREVENTION OF JAUNDICE

Due to the wide range of potential causes, it's not possible to prevent all cases of jaundice. However, there are four main precautions that you can take to minimise your risk of developing Jaundice. They are:

1. Ensuring that you stick to the recommended daily amount (RDA) for alcohol Consumption
2. Maintaining a healthy weight for your height and build.
3. If appropriate, ensuring that you're vaccinated against a Hepatitis A or B infection, vaccination would usually only be recommended depending on where in the world you're travelling .
4. Minimizing your risk of exposure to Hepatitis C because there's currently no vaccine for the condition.

MANAGEMENT

Treatment depends on the cause of the underlying condition leading to Jaundice and any potential complications related to it. Once a diagnosis is made, treatment can then be directed to address that particular condition, and it may or may not require hospitalization.

1. Treatment may consist of expectant management (watchful waiting) at home with rest.
2. Medical treatment with intravenous fluids, medications, antibiotics, or blood transfusions may be required.
3. If a drug/toxin is the cause, these must be discontinued.
4. In certain cases of newborn jaundice, exposing the baby to phototherapy or exchange blood transfusions may be required to decrease elevated bilirubin levels.
5. Surgical treatment may be required in case of Obstructive Jaundice.

REMOVAL OF OBSTRUCTIVE JAUNDICE

Non-surgical

Extracorporeal Shockwave Lithotripsy

- Non-invasive
- successive shock wave pressure pulses
 - fragment the stones into smaller pieces so they can easily pass through the duct

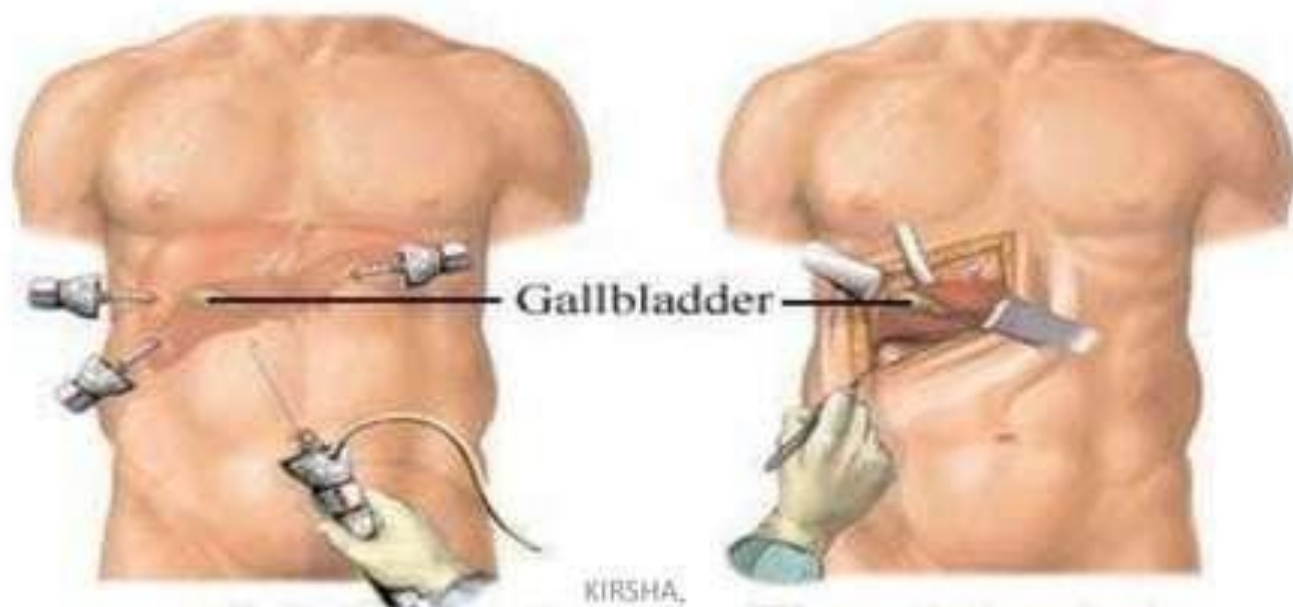
Endoscopic Retrograde Cholangiopancreatography

- insertion of the endoscope *up* into the ducts in a direction opposite to or against the normal flow of bile *down* the ducts (retrograde)

Surgical

Laparoscopic Cholecystectomy

- Minimally Invasive Surgery (MIS), Band-Aid Surgery, Keyhole Surgery, or Pinhole Surgery



TREATMENT

- Supportive care
- IV fluids in cases of dehydration
- Medications for nausea/vomiting and pain
- Antibiotics
- Antiviral medications such as Acyclovir
- Blood transfusions
- For Autoimmune Hepatitis- Steroids ,Immunosuppressants
- For Chronic Hepatitis B And C- Interferon
- For Fulminant Hepatitis And End Stage Liver Failure- Liver transplantation
- Liver Cancer- Chemotherapy /Radiation Therapy
- Neonatal Jaundice- Phototherapy