APPROACH TO A PATIENT WITH JAUNDICE

*Whether the hyperbilirubinemia is predominantly conjugated or unconjugated in nature.

*Whether other biochemical tests are abnormal.

*First step

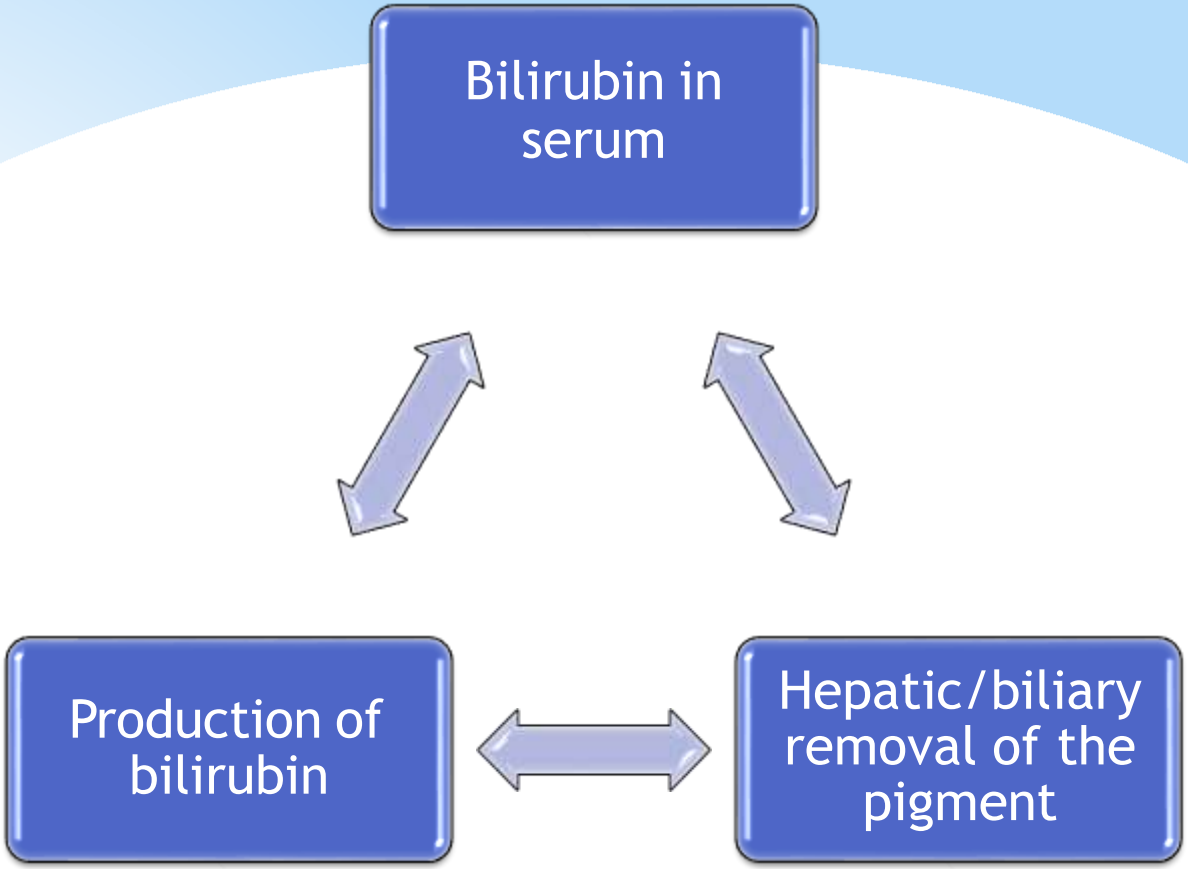
Isolated elevation of bilirubin

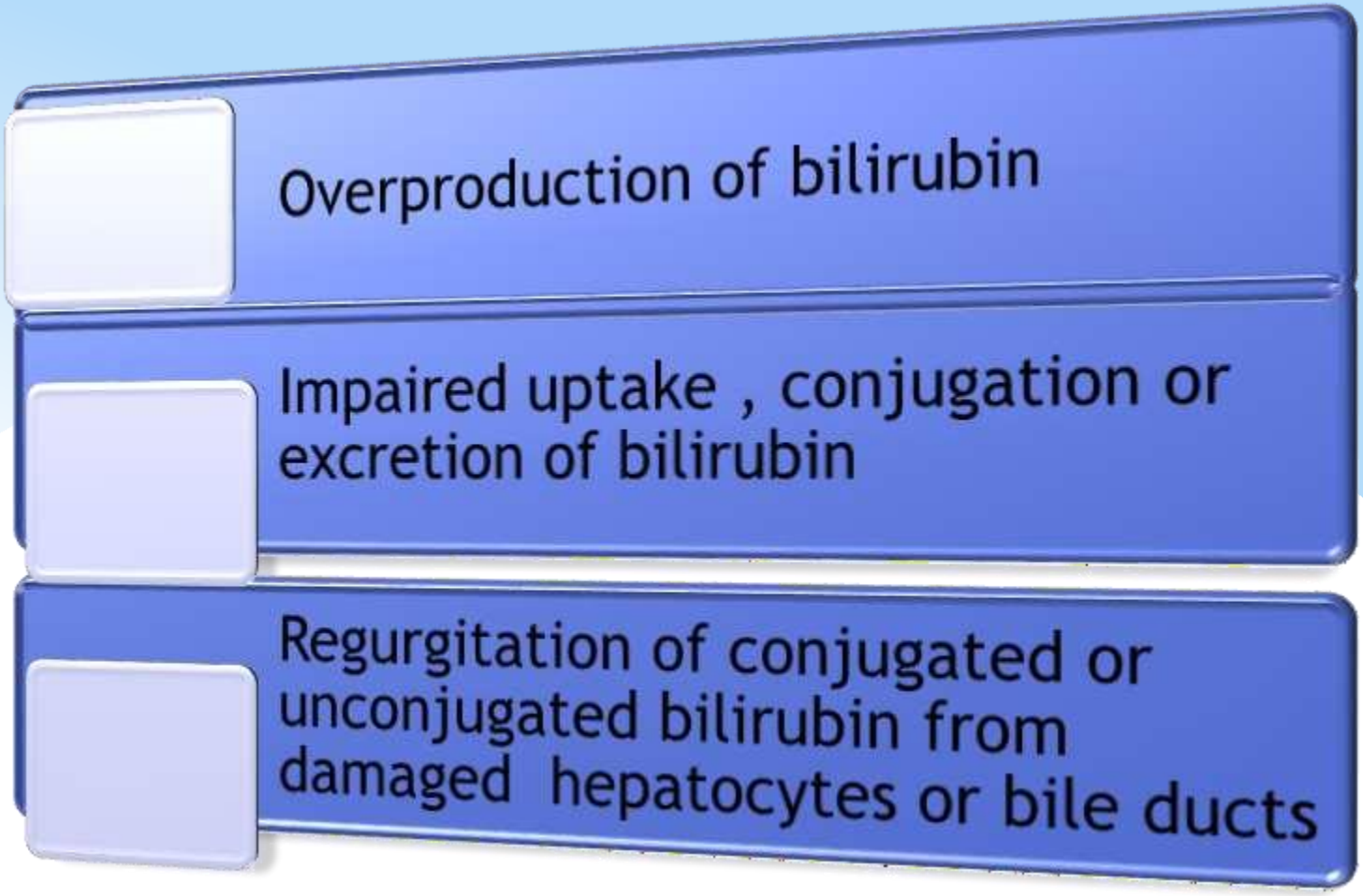
Elevation of serum bilirubin with other liver test abnormalities

Production of bilirubin

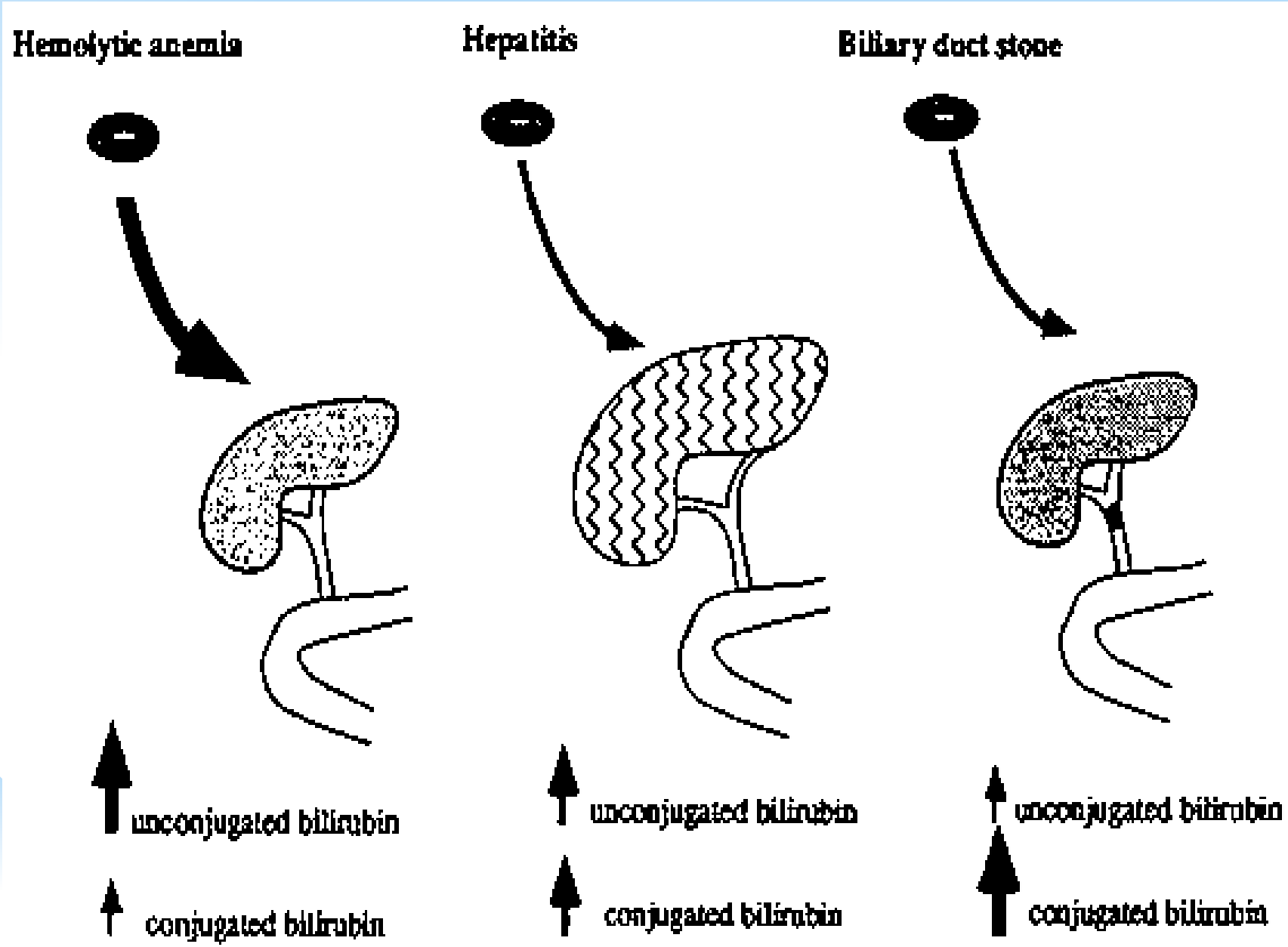
Hepatic/biliary removal

*Concept


Bilirubin in serum
Production of bilirubin
Hepatic/biliary removal of the pigment



*Hyperbilirubinemia


Hemolytic anemia
Hepatitis
Biliary duct stone
unconjugated bilirubin
conjugated bilirubin
unconjugated bilirubin
conjugated bilirubin
unconjugated bilirubin
conjugated bilirubin

*Unconjugated Hyperbilirubinemia

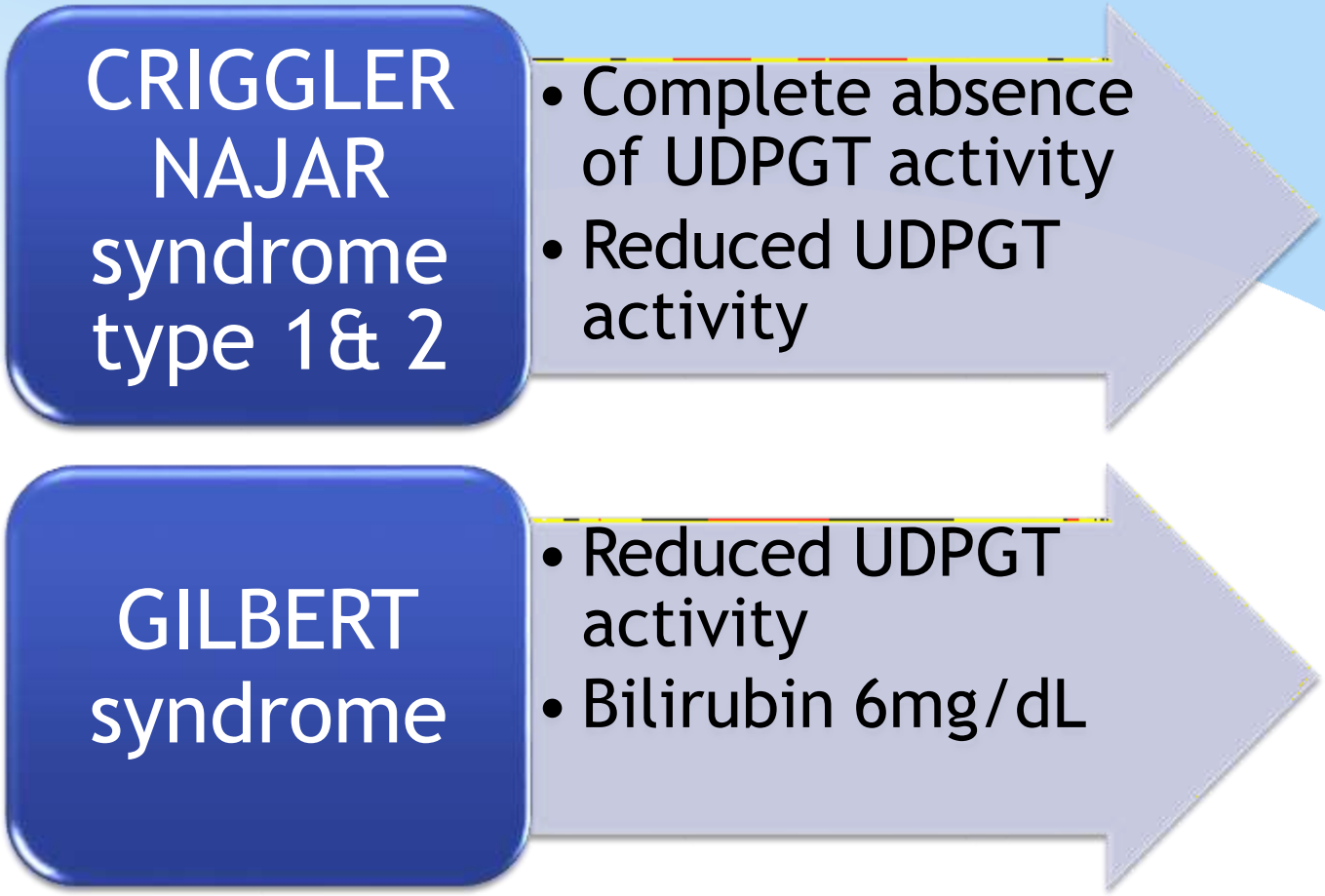
*Hemolytic process resulting in overproduction of bilirubin (HEMOLYTIC DISORDERS & INEFFECTIVE ERYTHROPOIESIS).

*Impaired uptake /conjugation of bilirubin(DRUG EFFECT or GENETIC DISORDERS)

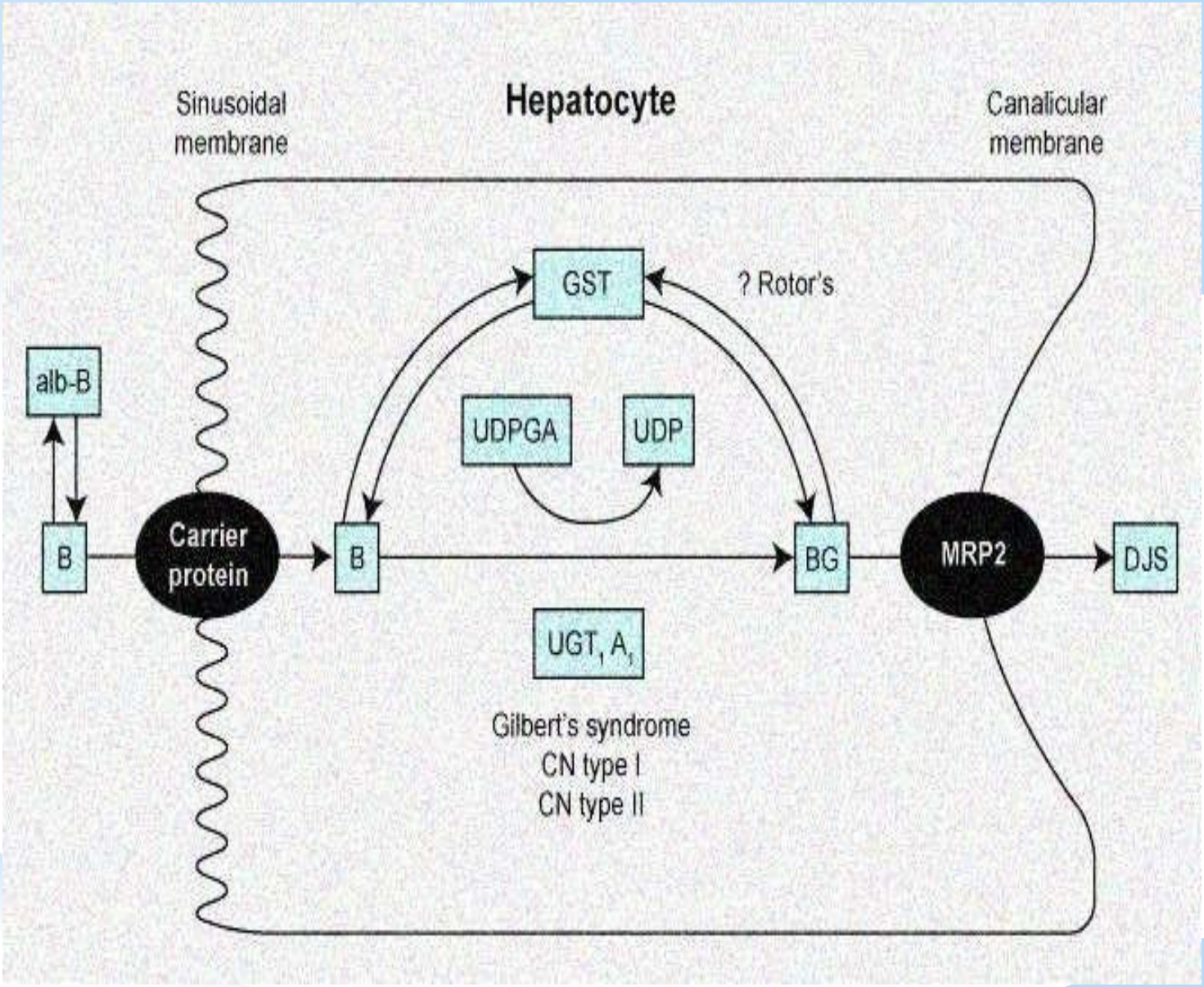
*Unconjugated Hyperbilirubinemia

CAUSES OF ISOLATED HYPERBILIRUBINEMIA

1. Indirect hyperbilirubinemia
    1. Hemolytic disorders
        1. Inherited
            1. Spherocytosis, elliptocytosis
            2. Glucose-6-phosphate dehydrogenase and pyruvate kinase deficiencies
            3. Sickle cell anemia
        2. Acquired
            1. Microangiopathic hemolytic anemias
            2. Paroxysmal nocturnal hemoglobinuria
            3. Spur cell anemia
            4. Immune hemolysis
            5. Parasitic infections
                1. Malaria
                2. Babesiosis
    2. Ineffective erythropoiesis
        1. Cobalamin, folate, thalassemia, and severe iron deficiencies
    3. Drugs
        1. Rifampicin, probenecid, ribavirin
    4. Inherited conditions
        1. Crigler-Najjar types I and II
        2. Gilbert's syndrome


CRIGGLER NAJAR syndrome type 1& 2
• Complete absence of UDPGT activity
• Reduced UDPGT activity
GILBERT syndrome
• Reduced UDPGT activity
• Bilirubin 6mg/dL

*syndromes


Sinusoidal membrane
Hepatocyte
Canalicular membrane
GST
? Rotor's
alb-B
UDPGA
UDP
B
Carrier protein
B
BG
MRP2
DJS
UGT, A,
Gilbert's syndrome
CN type I
CN type II

Differential Diagnosis of Hereditary Jaundice with Normal Liver Chemistries & No Signs or Symptoms of Liver Disease

Unconjugated Hyperbilirubinemia			
		Crigler-Najjar Syndrome	
	Gilbert's	Type I	Type II
Usual clinical features	Appear in early adulthood; often 1st re-cognized w/ fasting	Jaundice, kernicterus in infants, young adults	Asymptomatic jaundice, kernicterus rare
Liver biopsy	Normal	Normal	Normal
Treatment	Not needed	Liver transplant	Phenobarbital

Differential Diagnosis of Hereditary Jaundice with Normal Liver Chemistries & No Signs or Symptoms of Liver Disease

Unconjugated Hyperbilirubinemia			
		Crigler-Najjar Syndrome	
	Gilbert's	Type I	Type II
Incidence	<7% of pop'n	Very rare	Uncommon
Inheritance mode	AD	AR	AD
Serum bilirubin usual total (mg/dL)	<3; ≤6	>20	<20
	Mostly B1; inc. with fasting	All indirect	All indirect
Defect	Hepatic UDP-glucuronyl transferase activity		
	Decreased	Absent	Marked dec.
Age at onset of jaundice	Adolescence	Infancy	Childhood, adolescence

*Criggler twins

* Direct hyperbilirubinemia
  * **Inherited conditions**
    * Dubin-Johnson syndrome
      * Rotor's syndrome

* Conjugated hyperbilirubinemia

Dubin johnson syndrome

- Mutation in gene for multiple drug resistance protein 2

Rotor syndrome

- Problem with hepatic storage of bilirubin

*Conjugated Hyperbilirubinemia

* History

* Physical examination

* Lab tests

* Elevation of serum bilirubin with other LFT abnormalities

History

* Drugs.
* H/o transfusions, intravenous and intranasal drug use ,tattoos and sexual activity.
* H/o recent travel.
* H/o exposure to people with jaundice .
* H/o Exposure to contaminated foods.
* H/o Alcohol consumption.

*H/o myalgia , arthralgia ,rash.

*Anorexia , weight loss

*Abdominal pain

*Fever

*Pruritus

*Changes in urine and stool colour.

* Arthralgia and myalgia precluding jaundice- HEPATITIS(viral or drug related).

* Jaundice associated with sudden onset of severe RUQ pain and chills – CHOLEDOCHOLITHIASIS AND ASCENDING CHOLANGITIS.

* Diagnosis

Examination

* Temporal and Proximal muscle wasting – cirrhosis or pancreatic cancer.
* Features of Chronic liver disease.
* VIRCHOW'S NODE.
* Sister Mary Joseph's nodule.
* ELEVATED JVP, ASCITES, RIGHT PLEURAL EFFUSION - CONGESTION

*Clues to diagnosis

*Enlarged left lobe of liver – cirrhosis.

*Nodular liver or abdominal mass- malignancy.

*Enlarged tender liver- hepatitis viral or alcoholic , acutely congested liver.

*Murphy's sign- cholecystitis.

*Ascites + jaundice – cirrhosis or malignancy.

*Lab tests

*Patients with hepatocellular process- aminotransferases elevation disproportionate to ALP.

*Patients with a cholestatic process have disproportionate elevation of ALP compared to aminotransferases.

Aminotransferases elevation in hepatocellular

ALP elevation in Cholestasis

*SERUM ALBUMIN – A low serum albumin suggests a chronic process such as cirrhosis or cancer.

*PROTHROMBIN TIME – elevated PT indicates either vitamin K deficiency due to prolonged jaundice or malabsorption or significant hepatocellular dysfunction.

HEPATOCELLULAR CONDITIONS THAT MAY PRODUCE JAUNDICE

Viral hepatitis
- Hepatitis A, B, C, D, and E
- Epstein-Barr virus
- Cytomegalovirus
- Herpes simplex

Alcohol

Drug toxicity
- Predictable, dose-dependent, (e.g., acetaminophen)
- Unpredictable, idiosyncratic, (e.g., isoniazid)

Environmental toxins
- Vinyl chloride
- Jamaica bush tea—pyrrolizidine alkaloids
- Kava Kava
- Wild mushrooms—*Amanita phalloides* or *A. verna*

Wilson's disease

Autoimmune hepatitis

Viral hepatitis

Alcohol

DRUGS

TOXINS

Wilson's disease/Autoimmune Hepatitis

*Hepatocellular

Features

* Patients with alcoholic hepatitis will have AST :ALT ratio of 2:1

* AST rarely exceeds 300 U/L.

* Patients with hepatitis due to viral or toxin-related will have Aminotransferases > 500 U/L.

*Investigations

*IgM HAV.

*Hbs Ag.

*IgM anti Hbc.

*HCV RNA.

*Tests for EBV,CMV.

*Wilson's disease do Serum Ceruloplasmin level.

*Autoimmune hepatitis – ANA and specific immunoglobulins.

*Cholestatic conditions

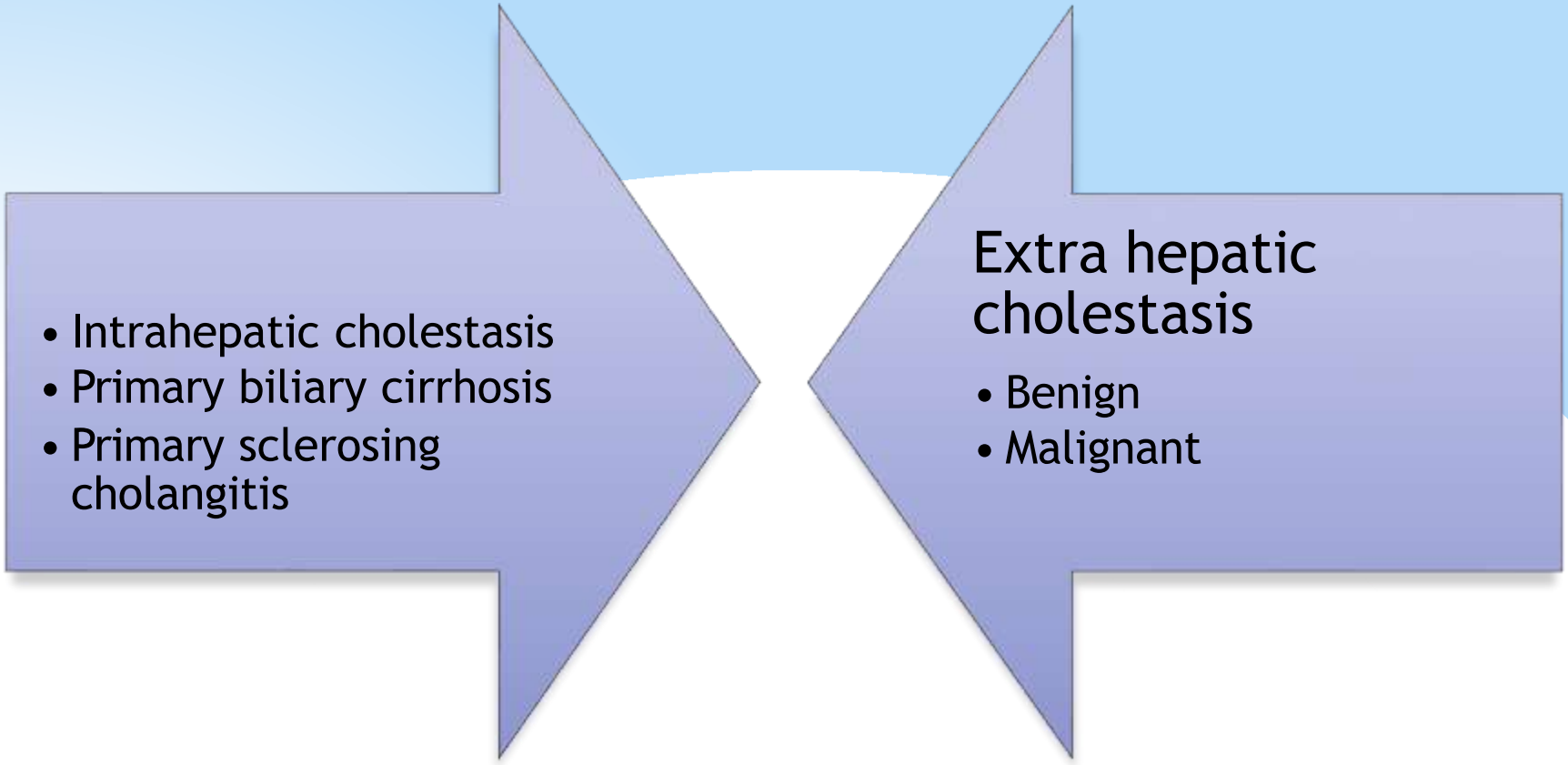
*Intrahepatic

*Extrahepatic

*Do an USG that will detect the presence of biliary dilatation.

*Biliary dilatation + = extrahepatic cholestasis

*Biliary dilatation - = intrahepatic cholestasis



*Cholestasis

CHOLESTATIC CONDITIONS THAT MAY PRODUCE JAUNDICE

1. Intrahepatic
    1. Viral hepatitis
        1. Fibrosing cholestatic hepatitis—hepatitis B and C
        2. Hepatitis A, Epstein-Barr virus, cytomegalovirus
    2. Alcoholic hepatitis
    3. Drug toxicity
        1. Pure cholestasis—anabolic and contraceptive steroids
        2. Cholestatic hepatitis—chlorpromazine, erythromycin estolate
        3. Chronic cholestasis—chlorpromazine and prochlorperazine
    4. Primary biliary cirrhosis
    5. Primary sclerosing cholangitis
    6. Vanishing bile duct syndrome
        1. Chronic rejection of liver transplants
        2. Sarcoidosis
        3. Drugs

1. Inherited
    1. Progressive familial intrahepatic cholestasis
2. Benign recurrent cholestasis
2. Cholestasis of pregnancy
3. Total parenteral nutrition
4. Nonhepatobiliary sepsis
5. Benign postoperative cholestasis
6. Paraneoplastic syndrome
7. Venoocclusive disease
8. Graft-versus-host disease
9. Infiltrative disease
    1. TB
    2. Lymphoma
    3. Amyloidosis

Intrahepatic cholestasis

* Hepatitis B, Hepatitis C can cause a cholestatic hepatitis.

* Hepatitis A , CMV, EBV, alcoholic hepatitis can also produce cholestatic picture.

* Primary biliary cirrhosis –Antimitochondrial antibody.

* Primary sclerosing cholangitis- multiple strictures of bile ducts with dilatation proximal to strictures.

*Distal CBD is an area that is difficult to be visualized by USG.

*CT scan .

*MRCP (Magnetic resonance cholangiography).

*ERCP(Endoscopic Retrograde Cholangio Pancreatography).

*Extrahepatic cholestasis

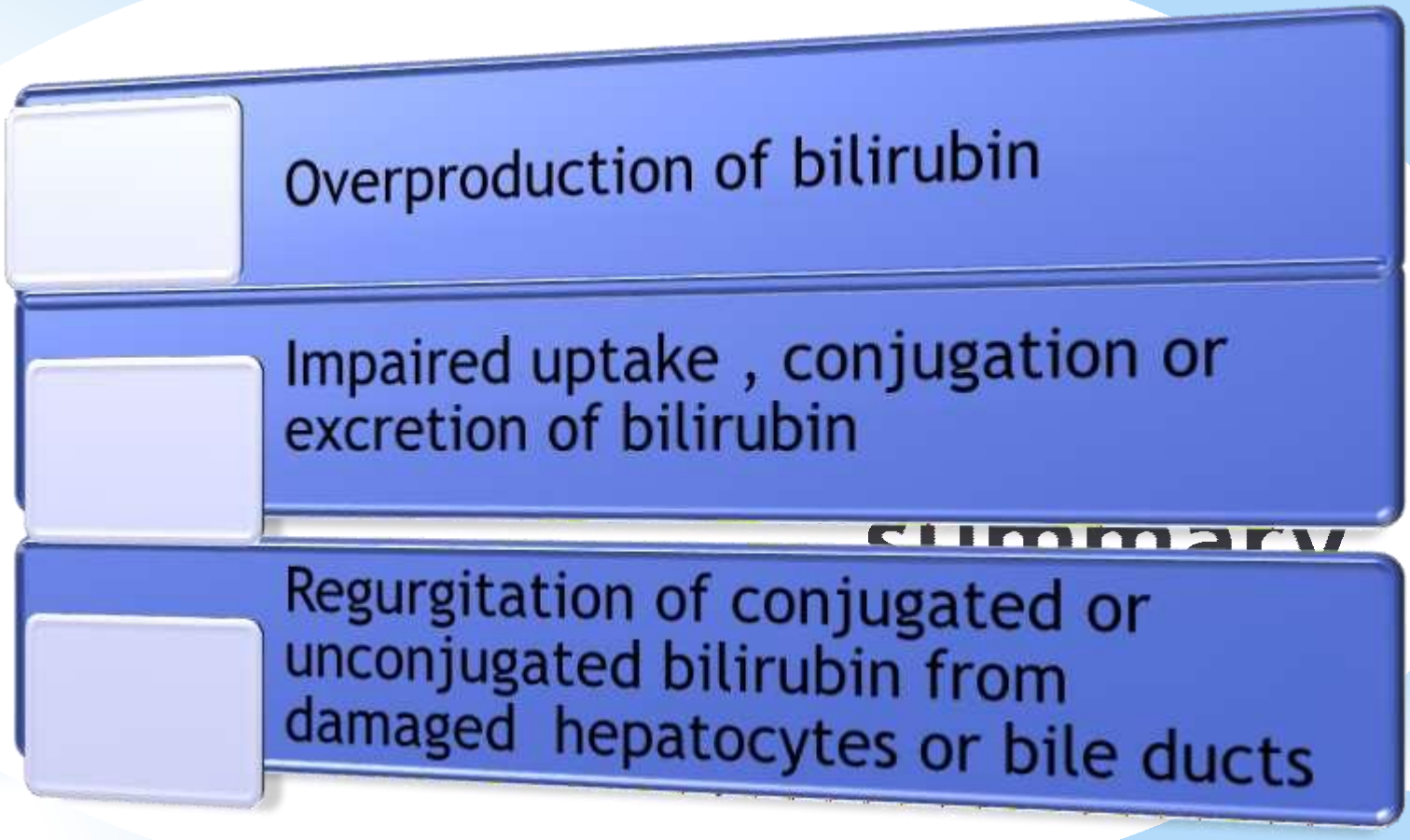
*Extra hepatic cholestasis

*Benign and malignant cause.

*Malignant causes include Pancreatic, Gall bladder , Ampullary and cholangiocarcinoma.

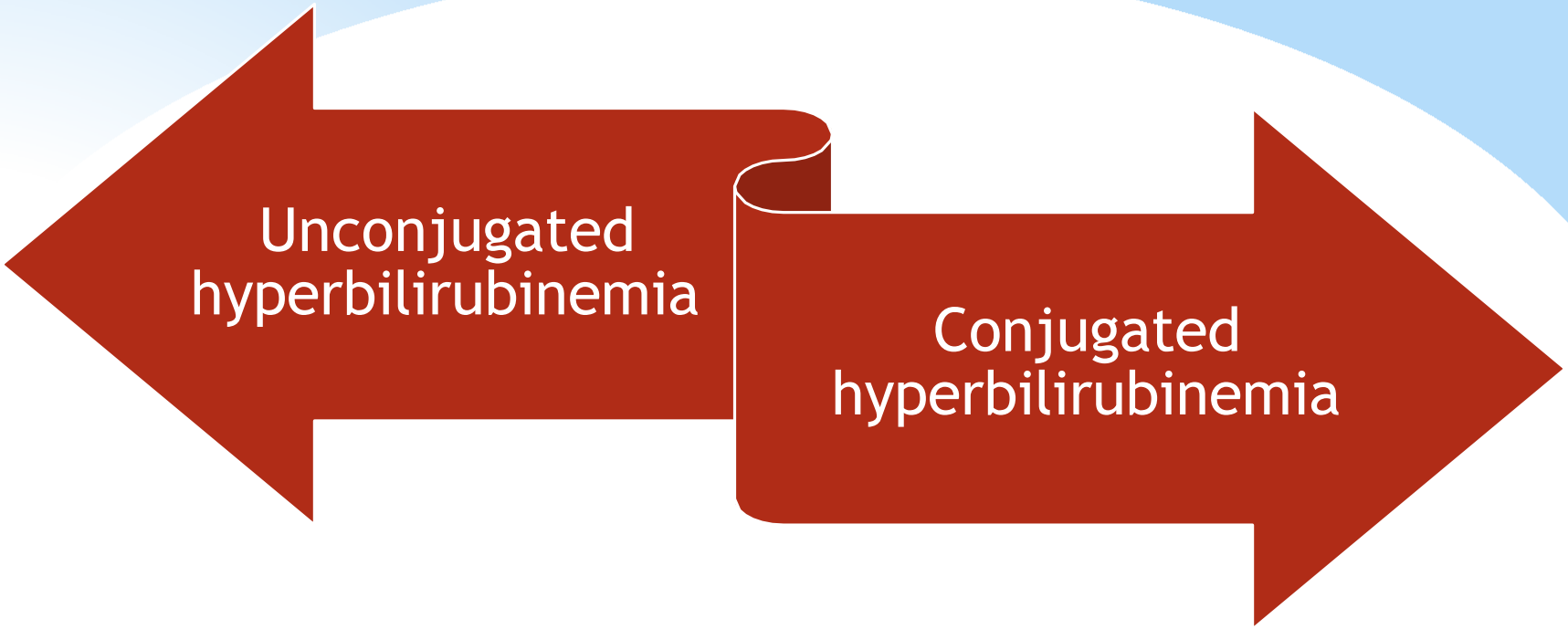
* Extrahepatic
  * Malignant
    * Cholangiocarcinoma
    * Pancreatic cancer
    * Gallbladder cancer
    * Ampullary cancer
    * Malignant involvement of the porta hepatis lymph nodes
  * Benign
    * Choledocholithiasis
    * Postoperative biliary structures
    * Primary sclerosing cholangitis
    * Chronic pancreatitis
    * AIDS cholangiopathy
    * Mirizzi syndrome
    * Parasitic disease (ascariasis)

SUMMARY


Overproduction of bilirubin
Impaired uptake , conjugation or excretion of bilirubin
Regurgitation of conjugated or unconjugated bilirubin from damaged hepatocytes or bile ducts

Isolated elevation of bilirubin

Elevation of serum bilirubin with other liver test abnormalities


Unconjugated hyperbilirubinemia
Conjugated hyperbilirubinemia

*Unconjugated Hyperbilirubinemia

Dubin Johnson syndrome

Rotor syndrome

*Conjugated hyperbilirubinemia

Viral hepatitis

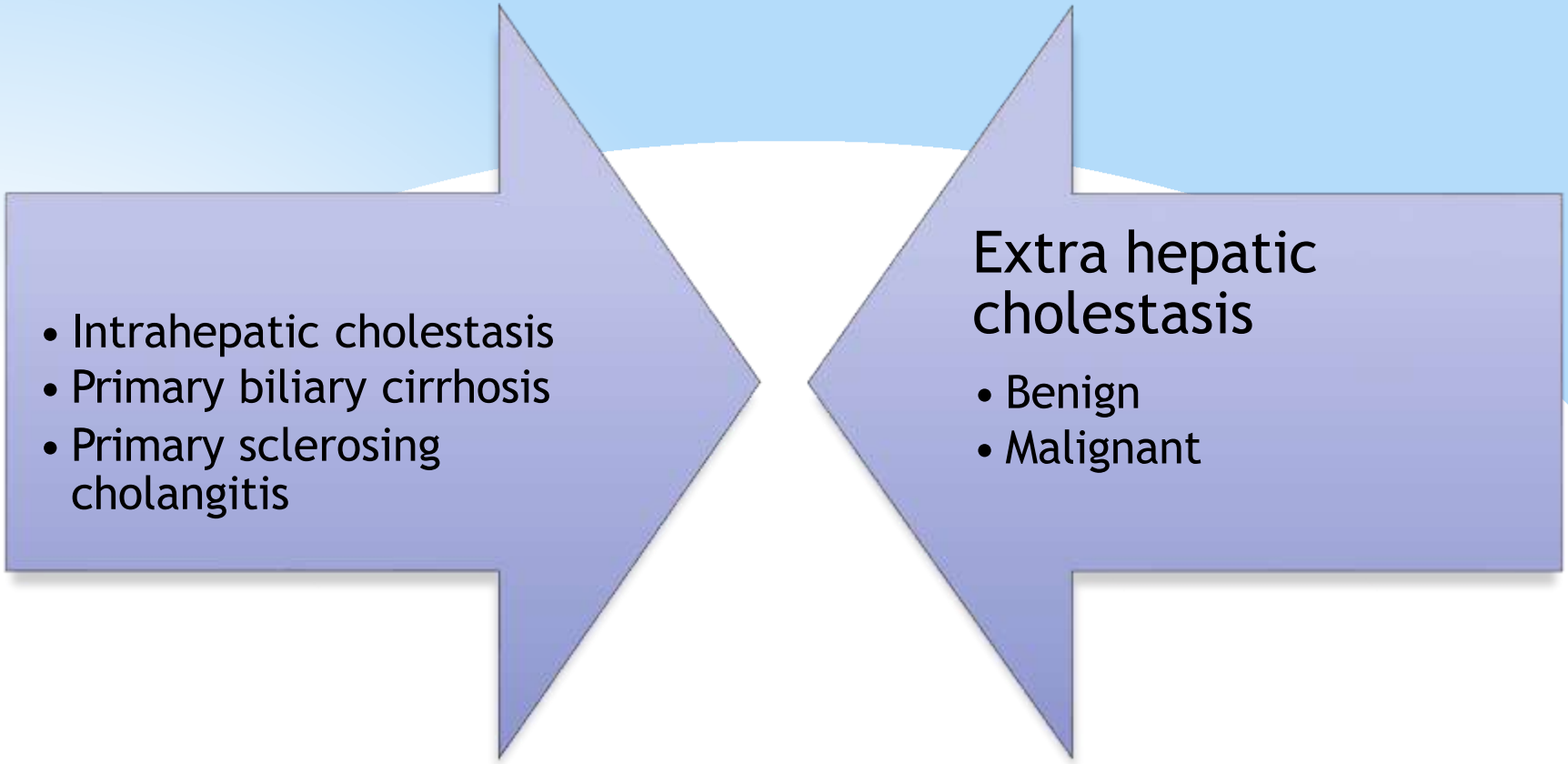
Alcohol

DRUGS

TOXINS

Wilson's disease/Autoimmune Hepatitis

*Hepatocellular



*Cholestasis

*Total bilirubin- 6.3mg/dl.

*Direct bilirubin – 3.9 mg/dl.

*Indirect bilirubin- 2.4 mg/dl.

*LFT

*SGOT – 292 U/L.

*SGPT – 542 U/L.

*ALP – 60 U/L.

*TOTAL PROTEIN – 5.6 gm/dl.

*Albumin – 3.7 gm/dl.

*Globulin 1.9 gm/dl.

*A/G ratio 1.9:1


THANK YOU