



12 CAUSES AND PATHOGENESIS OF JAUNDICE



GIT

Learning objectives :

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

Hyperbilirubinemia (Jaundice, Icterus):

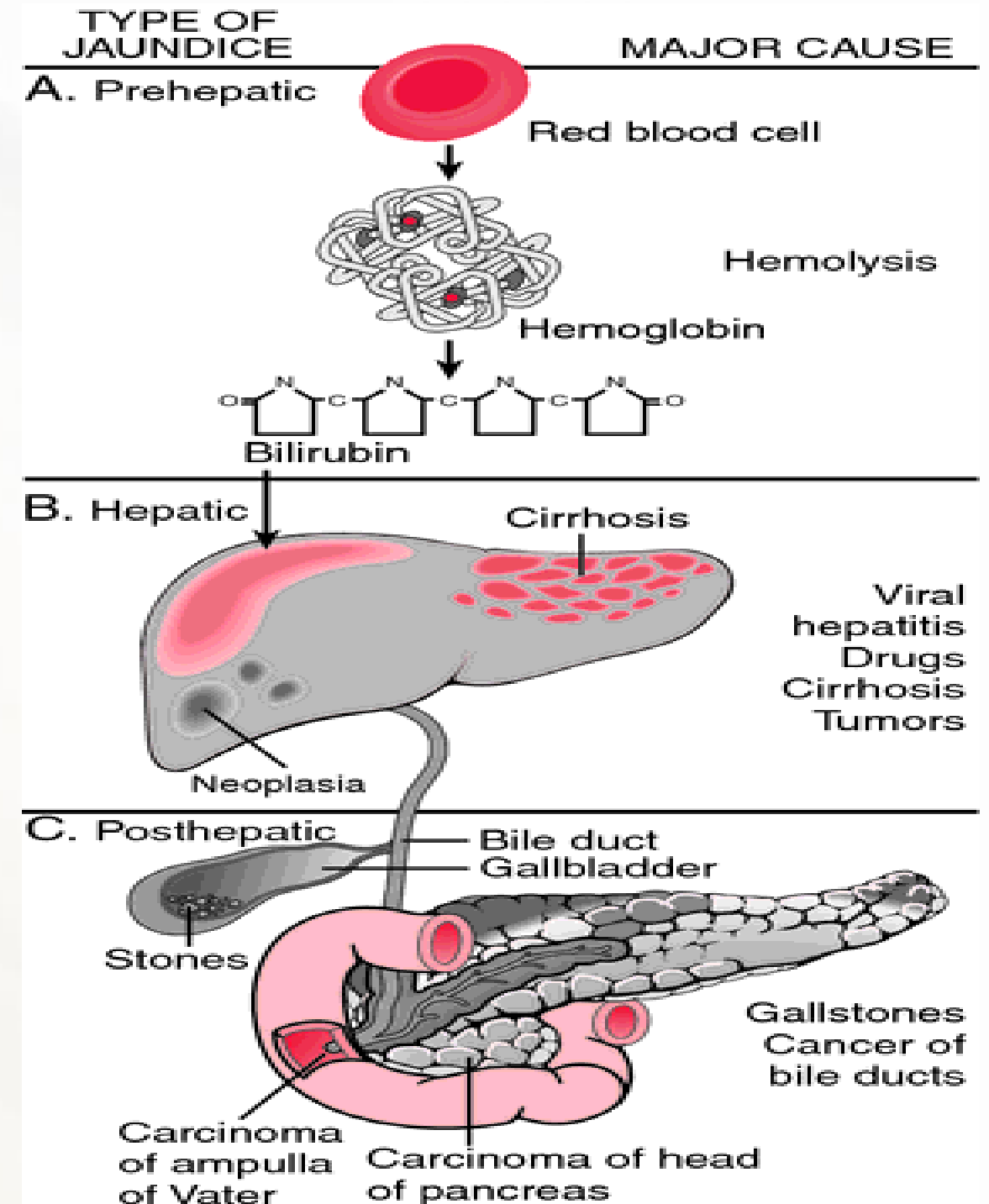
- **Jaundice** : It is the yellow coloration of the skin, sclera, mucous membranes and deep tissues.
- The usual cause is **large quantities of bilirubin in the ECF**, either free or conjugated bilirubin.
- The **normal** plasma concentration of total bilirubin is **0.5 mg/dl**. (0.3-1.2 mg/dl of Blood)
- 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 $\mu\text{mol/l}$). **(clinical)**
- Bilirubin level from **0.5 to 2 mg/dl** is called **subclinical jaundice**. **(has jaundice but can't be seen)**

Classification of jaundice:

♠ Prehepatic (hemolytic) jaundice

♠ Hepatic (hepatocellular) jaundice

♠ Posthepatic (obstructive) jaundice



Prehepatic (hemolytic) Jaundice

Causes	<ul style="list-style-type: none">• In hemolytic jaundice, the excretory function of the liver is not impaired.• It results from excess production of bilirubin (beyond the liver's ability to conjugate it) following hemolysis.• Excess RBC lysis is commonly the result of:<ul style="list-style-type: none">• Autoimmune disease• Hemolytic disease of the newborn• Rh- or ABO- incompatibility• Structurally abnormal RBCs (Sickle cell disease)• Breakdown of extravasated blood
Plasma bilirubin	The plasma concentrations of free bilirubin (hemobilirubin) rises to levels much above normal but it is not filtered through the kidney .
Urine bilirubin	The urine is free from bilirubin (acholuric jaundice)
Van der Bergh reaction	is indirect .
Stools color	The stools appear darker than the normal color due to excessive stercobilin formation.

Hepatic (hepatocellular) Jaundice

<p>Causes</p>	<ul style="list-style-type: none"> ◆ Hyperbilirubinemia may be due to: <ul style="list-style-type: none"> • <u>Impaired uptake of bilirubin into hepatic cells.</u> • <u>Disturbed intra cellular protein binding or conjugation.</u> • <u>Disturbed active secretion of bilirubin into bile canaliculi.</u> ◆ The causes may be due to: <ul style="list-style-type: none"> • 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
<p>Plasma bilirubin</p>	<ul style="list-style-type: none"> • The diseased liver cells are unable to take all the <u>unconjugated</u> hemobilirubin formed, increasing its concentration in the blood. • Also, there is intrahepatic biliary duct obstruction that leads to regurgitation of <u>conjugated</u> bilirubin to blood. <p>◆ Both types of bilirubin (conjugated & unconjugated) are present in blood in high concentration.</p>
<p>Urine bilirubin</p>	<p>Urine appears <u>dark brown</u> due to filtration of <u>excess conjugated bilirubin</u> through the kidney.</p>
<p>Van der Bergh reaction</p>	<p>is biphasic</p>
<p>Stools color</p>	<p>Stools appear <u>pale grayish</u> in color due to deficiency of stercobilin.</p>

Continue; Hepatic (hepatocellular) Jaundice :

◆ In this case, **hyperbilirubinemia** is usually accompanied by **other abnormalities** in biochemical markers of liver function:

1. Alanine aminotransferase (ALT), serum glutamic pyruvic transaminase (SGPT)

- Cholestatic obstruction : ALT goes up and down (pulsatile increase)
- Hepatic jaundice : ALT persistent increase for a long period of time (months)

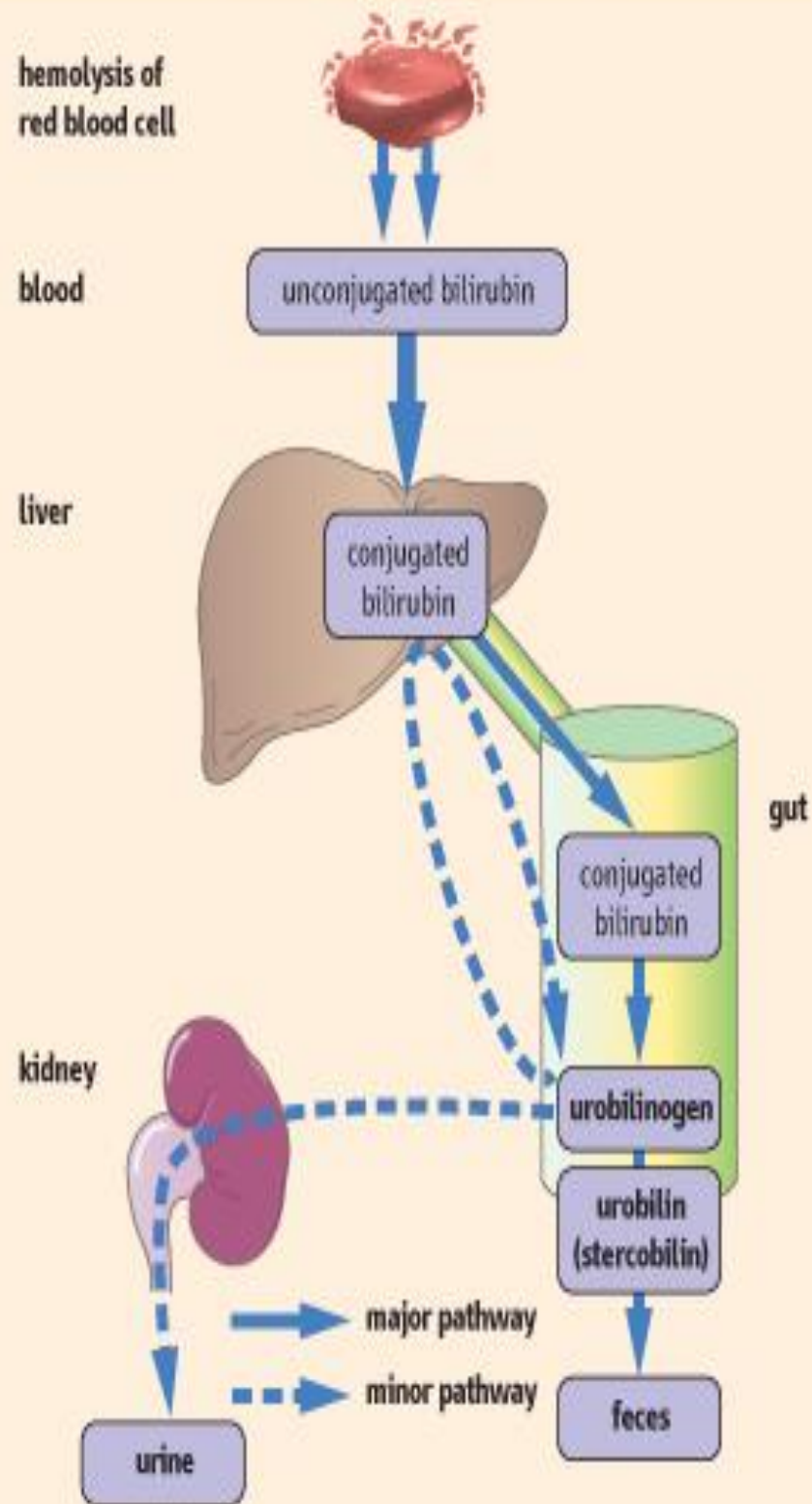
2. Aspartate aminotransferase (AST), serum glutamic oxaloacetic transaminase (SGOT).

3. alkaline phosphatase (ALP) and Gamma-glutamyltransferase (γ GT).

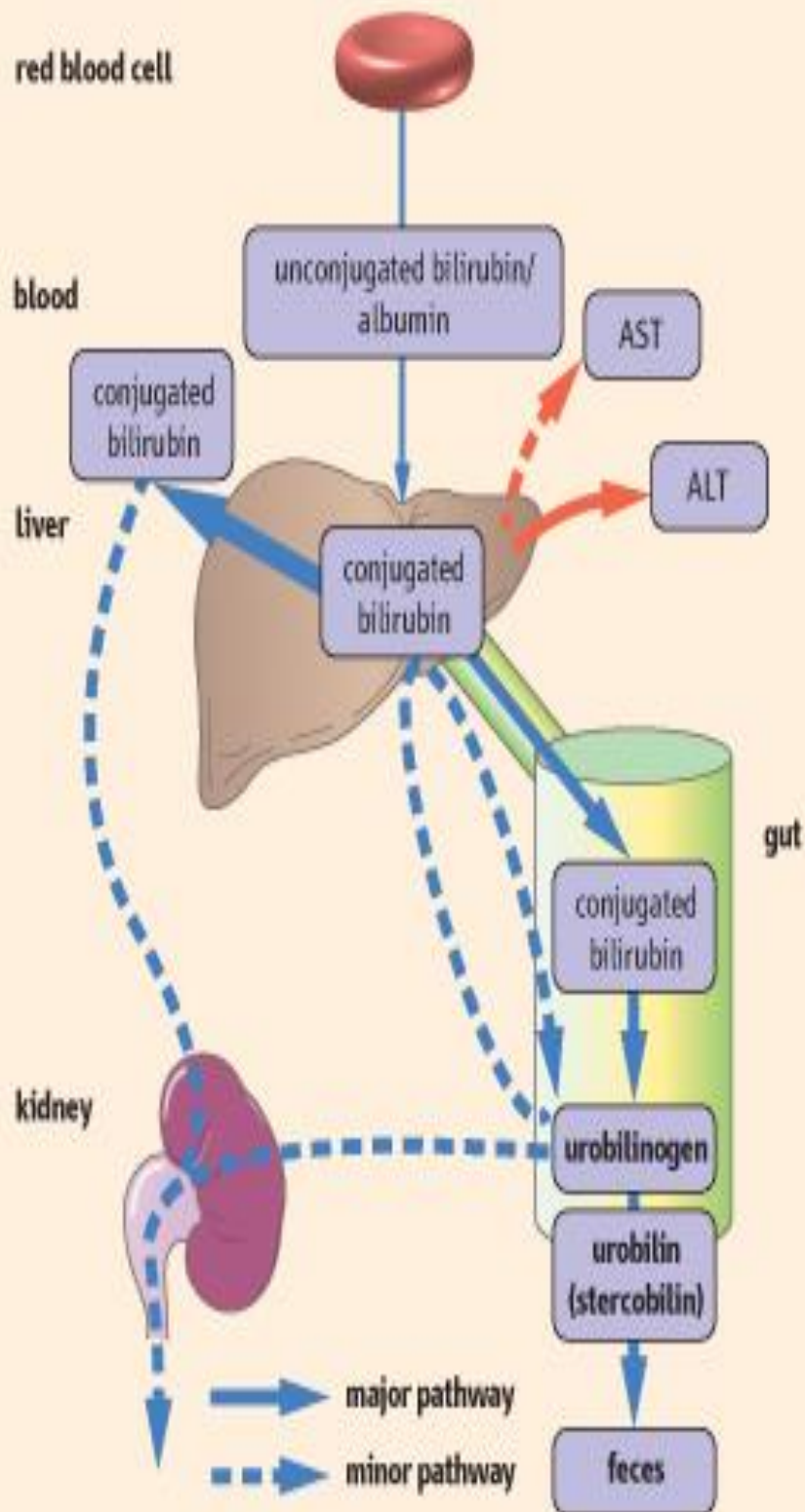
Posthepatic (obstructive) jaundice

Causes	Caused by an obstruction of the biliary tree : 1- Intrahepatic bile duct obstruction e.g. <ul style="list-style-type: none">• Drugs• Primary biliary cirrhosis• Cholangitis. 2- Extrahepatic bile duct obstruction e.g. <ul style="list-style-type: none">• Gall stones.• Cancer head pancreas.• Cholangiocarcinoma.
Plasma bilirubin	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 .
Urine bilirubin	conjugated bilirubin is filtered through the kidney and appears in urine giving it dark brown (liquorice) color. Urine is free from Urobilinogen
Van der Bergh reaction	is direct .
Stools color	Stools are clay color due to absence of Stercobilin

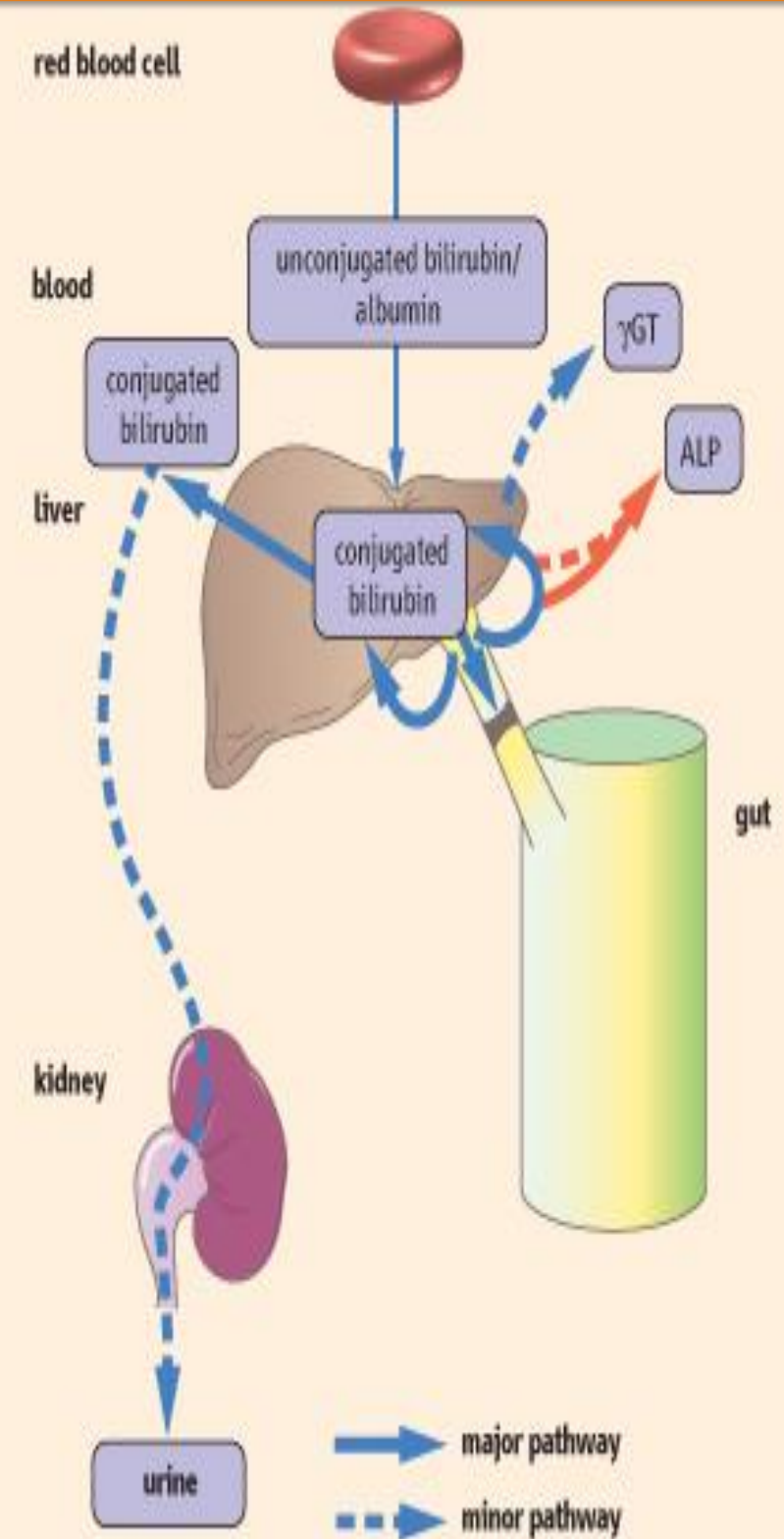
Prehepatic (hemolytic) jaundice



intrahepatic jaundice



Posthepatic (obstructive) 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
- 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 than 10 days** to resolve is usually pathological, needs to be investigated.

Gallstone formation:

Males' Slide

- 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.

Summary

	Prehepatic (hemolytic)	Hepatic (hepatocellular)	Posthepatic (obstructive)
Unconjugated	↑	↑	Normal
Conjugated	Normal	↑	↑
VDB	Indirect	Biphasic	Direct
AST & ALT	Normal	↑	Normal
ALP & γGT	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 Reaction ALT= Alanine amine transferase liquorice= very dark

AST = Aspartate amine transferase γGT= Gamma glutamyl transpeptidase



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GOOD LUCK