LIVER FUNCTION TESTS

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Liver function tests

- Total Bilirubin 0.2 to 0.9 mg/dl
- Conjugated bilirubin 0 to 0.2 mg/dl
- Total protein 6 – 8 gm/dl
- Albumin 3.5 – 5 gm/dl
- Prothrombin time 11 to 12 seconds
- **Aspartate transferase (AST) GOT 10-35 U/L**
- **Alanine transferase (ALT) GPT 10-45 U/L**
- **Alkaline phosphatase ALP 25-100 U/L**
- **γ-Glutamyl transferase GGT male 5-45 U/L female 5-30 U/L**
- **5' – Nucleotidase 3-9 U/L**

Classification of liver function tests

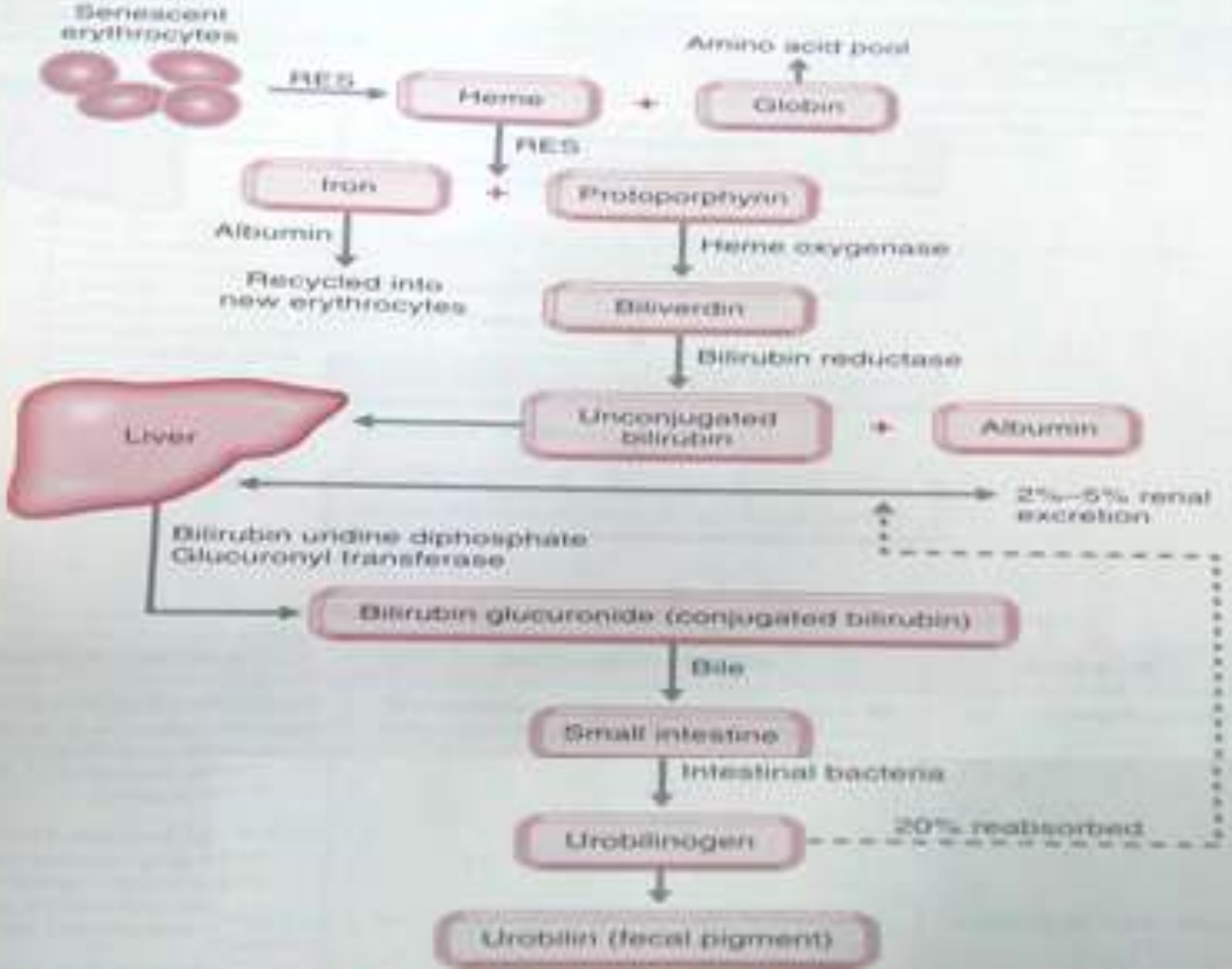
- Tests based on the excretory function: bilirubin
- Tests based on of synthetic function (plasma proteins and coagulation factors)
- **Indicators of cell damage (transaminases)**
- **Indicators of cholestasis (ALP, GGT, 5 nucleotidase)**
- Tests indicating etiology:

✓ Hepatitis markers

✓ α1- antitrypsin

✓ α1-Fetoprotein (HCC)

✓ Ceruloplasmin, copper in serum and urine (Wilson's dis.)


Senescent erythrocytes
RES
Heme
Amino acid pool
Globin
RES
Iron
Protoporphyrin
Albumin
Heme oxygenase
Recycled into new erythrocytes
Biliverdin
Bilirubin reductase
Liver
Unconjugated bilirubin
Albumin
2%–5% renal excretion
Bilirubin uridine diphosphate Glucuronyl transferase
Bilirubin glucuronide (conjugated bilirubin)
Bile
Small intestine
Intestinal bacteria
Urobilinogen
20% reabsorbed
Urobilin (fecal pigment)

Jaundice

Clinical jaundice appears when bilirubin concentration is more than 3 mg/dl.

Levels between 1 and 3 mg/dl is sub-clinical jaundice.

Classification of Jaundice:

Prehepatic or Hemolytic jaundice

Hepatocellular jaundice

Post hepatic or Obstructive jaundice

- In hemolytic jaundice

Increased production of unconjugated bilirubin from hemolysis at rates that exceed the ability of the liver to clear it

Increased production of bilirubin causes increased formation of urobilinogen which appears in the urine.

Hepatocellular jaundice

Elevation of both unconjugated and conjugated bilirubin **(BiPhasic)**

Obstructive jaundice:

Decreased secretion of conjugated bilirubin into canaliculi lead to increase direct bilirubin & presence of bilirubin in urine and absence of urobilinogen in urine

Intrahepatic obstruction by drugs , cirrhosis.

Extra hepatic obstruction - stones , Carcinoma.

SERUM ALBUMIN

- Plasma proteins synthesized exclusively by liver
- Albumin half life is about 21 days
- Due to its slow turn over – not a good indicator of acute or mild hepatic dysfunction
- Non hepatic causes of Hypoalbuminemia -
- Protein losing enteropathy
- Nephrotic syndrome

- Low serum albumin level is commonly observed in severe liver disease.

Prothrombin time

- With the exception of VWF , all other factors are synthesized in liver
- PT measure the activity of factors I,II, V,VII &X
- Because of great functional reserve of liver, failure of hemostasis occurs in sever or long standing liver dis.
- In cholestasis deficiency of vit k cause prolongation of PT but corrected by iv injection of vit. k

Indicators of cell damage (transaminases)

- AST(SGOT) – found in liver> cardiac muscle > skeletal muscle> kidneys >brain & erythrocytes.
- ALT(SGPT) – found primarily in liver
- When there is damage to liver cell membrane – increased permeability and so increased serum concentration

Clinical significance

- ALT is liver specific enzyme

- In most acute hepatocellular disorders ALT is higher than AST except in:
- 1-Cirrhosis
- 2-Alcoholic hepatitis
- 3-Liver neoplasia

- Levels of >1000 IU/L occurs in –
- Acute viral hepatitis
- Toxin and drug induced hepatitis
- Ischaemic liver injury

- ALT is present in the cytosol of hepatocytes.
- AST is present both in the cytosol and mitochondria of the hepatocytes.

2 forms of AST are known-

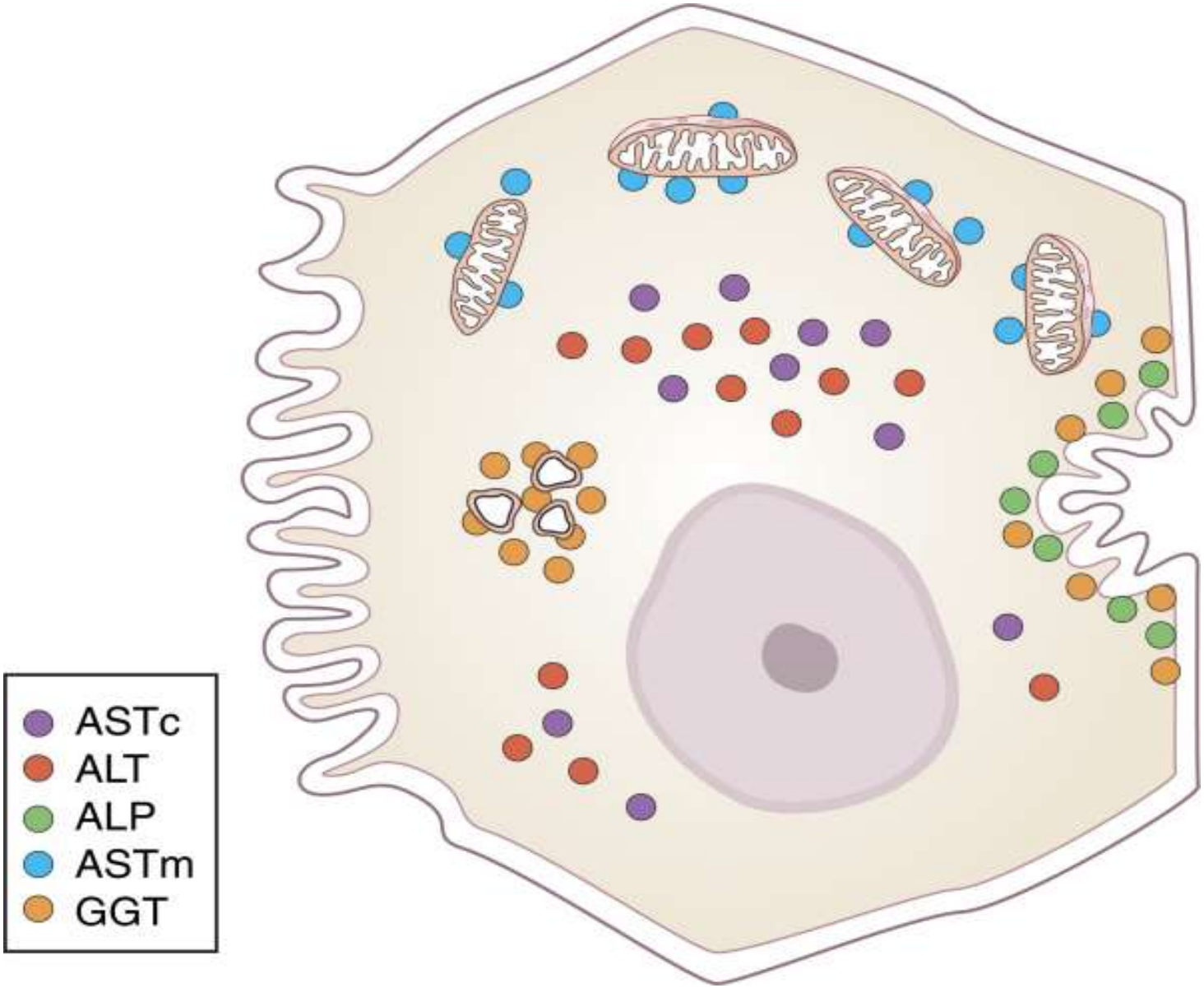
1. Cytosolic
2. Mitochondrial (mAST)

- Accounts for 80% of total AST activity within liver cells

Isolated AST elevation

1. Alcohol -related
2. Drug -induced liver injury,
3. Hemolysis & hemolytic anemia
4. AMI
5. Acute pancreatitis

- Determination of these enzymes are helpful in distinguishing hepatocellular from cholestatic jaundice
- Increase in AST and ALT is much more (>500 IU/L)in hepatocellular jaundice than in cholestatic jaundice
- Persistence of elevated ALT and AST beyond 6 months in a case of hepatitis indicates development of chronic hepatitis


ASTc
ALT
ALP
ASTm
GGT

ENZYMES WHOSE ELEVATION REFLECTS CHOLESTASIS

1. Alkaline phosphatase (ALP)
2. 5'nucleotidase (5'NT)
3. Gamma glutamyl transferase (GGT)

- ALP – found in liver found in bile canaliculi.
- Other important sources of ALP is bone, placenta and small intestine
- Physiological increase in ALP is seen in –

- During periods of physiological bone growth
- Healing of bone fractures
- Pregnancy

- ALP >4 times the Normal is seen in –

1. Cholestatic liver disease
2. Bone disorder like rickets, Paget's disease of bone

- ALP isoenzymes: (liver, bone, intestine & placenta), there is another form identical to placental isoenzyme present with malignancy called regan

- If an isolated increase in ALP is seen , identification of the source of elevated isoenzyme is helpful by:

1. Fractionation of ALP by electrophoresis
2. Different isoenzymes have diiferent susceptibility to inactivation by heat
   - heat stable fraction–placenta isoenzyme
   - Most sensitive to heat inactivation is – bone ALP

3. Measure serum levels of GGT and 5'NT – they are elevated in only liver disease

- **γ-Glutamyl transferase**

In the liver it located in the canaliculi and in microsome of hepatic parenchyma.

- Serum GGT is increased in –

1. Alcoholism- Is a helpful clue in suspected cases of alcoholism (even in absence of alcoholic liver disease)

2. Cholestasis (not elevated in bone diseases or pregnancy)

- GGT and 5'NT is especially used to assess the nature of ALP

5’ – Nucleotidase

It is elevated in obstructive jaundice.

Advantage of this enzyme is that it is not elevated in bone disease.

Can differentiate bone and liver elevation with ALP.

Some of liver diseases:

Cirrhosis

- Decrease albumin
- Increase globulins
- Inverted A/G ratio
- Decrease cholesterol
- Prolonged prothrombin time

Acute hepatitis

- Increaase bilirubin mainly direct bilirubin but may be indirect in 15% of cases.
- Marked increase ALT & AST, before clinical sym., reach peak about one week then gradually decrease to reach normal level about one month.
- Persistence of increase enzymes more than 6 month → chronic hepatitis

Cholestatic liver diseases

- Increase direct bilirubin
- Bilirubinuria
- Pale stool & absent urobilinogen
- Increase ALP, GGT & 5-nucleotidase
- hypercholesterolemia
- Increase bile acid in plasma
- Malabsorption of fat &fat soluble vit.

Primary biliary cirrhosis

- Autoimmune dis. destruct intrahepatic ducts
- Female predominance
- 95% of pt. have antimitochondrial antibodies

Primary sclerosing cholangitis

- Autoimmune dis. Chronic inflamation of intra hepatic & extrahepatic bile duct
- Male predominance
- Have perinuclear antineutrophil cytoplasmic(p-ANCA), antinuclear(ANA) & anti-smooth muscle antibodies(ASMA)

Report

		Serum Level	Unit
Total bilirubin	:	**0.6**	mg/dl
Direct bilirubin	:	**0.1**	mg/dl
Total protein	:	**7.1**	g/dl
Albumin	:	**4.3**	g/dl
AST (SGOT)	:	**18**	IU/l
ALT (SGPT)	:	**19**	IU/l
Alkaline phosphatase	:	**69**	IU/l

Report

		Serum Level	Unit
Total bilirubin	:	**9**	mg/dl
Direct bilirubin	:	**5.8**	mg/dl
Total protein	:	**7.9**	g/dl
Albumin	:	**4.4**	g/dl
AST (SGOT)	:	**600**	IU/l
ALT (SGPT)	:	**950**	IU/l
Alkaline phosph.	:	**300**	IU/l

Report

		Serum Level	Unit
Total bilirubin	:	**10**	mg/dl
Direct bilirubin	:	**7.7**	mg/dl
Total protein	:	**7.8**	g/dl
Albumin	:	**4.2**	g/dl
AST (SGOT)	:	**14**	IU/l
ALT (SGPT)	:	**20**	IU/l
Alkaline phosphatase	:	**550**	IU/l

Report

		Serum Level	Unit
Total bilirubin	:	**1.2**	mg/dl
Direct bilirubin	:	**0.8**	mg/dl
Total protein	:	**6.7**	g/dl
Albumin	:	**2**	g/dl
AST (SGOT)	:	**50**	IU/l
ALT (SGPT)	:	**30**	IU/l
Alkaline phosphatase	:	**80**	IU/l

Report

		Serum Level	Unit
Total bilirubin	:	**12**	mg/dl
Direct bilirubin	:	**1.2**	mg/dl
Total protein	:	**6.7**	g/dl
Albumin	:	**3.4**	g/dl
AST (SGOT)	:	**12**	IU/l
ALT (SGPT)	:	**6**	IU/l
Alkaline phosphatase	:	**65**	IU/l

THANK YOU