Liver Functions

The major Functions

1) carbohydrate metabolism.
   A) Gluconeogenesis
   B) Glycogen synthesis & metabolism.

2) Fat metabolism.
   A) Fatty acid synthesis
   B) Cholesterol synthesis & excretion
   C) Lipoprotein synthesis..
   D) Ketogenesis (converting)
   The fatty acid ketone bodies.

3) Protein metabolism.
   A) Synthesis of plasma proteins.
   B) Urea synthesis.

4) Hormone metabolism.
   Metabolism, conjugation & excretion of steroidal & poly peptide hormones.

5) Drugs & foreign compounds; metabolism & excretion of drugs.
6) Liver is a good part in storage of:
   a) glycogen
   b) VIT A
   B) VIT B12
   C) Iron.

7) Also liver plays a good part in metabolism & secretion of Bilirubin. Therefore, any damage to the liver organ may affect any of the above functions.

The most important tests used in the diagnosis of liver diseases are S. Got, S. Gpt, T.S. Bilirubin, T.S. Protein & alkaline phosphates.

The most common diseases affecting the liver are:

1) Hepatitis: damage to the liver cells.
2) Cirrhosis: In this case an increase in the fibrous tissue formation result in shrinkage of the liver & a decrease in the hepatocellular function.

3) Tumours: most frequently are secondary. Metastases from cancers of the large bowel, stomach & the bronchus.

4) Obstruction of the bile flow: This due to pathological diseases or presence of stones.
Jaundice:
It’s the yellowish discoloration of the tissue due to the deposition of Bilirubin. the state indicated when the value is $0.2 \text{mg.}/100 \text{ml.}$ or more.

Hyper Bilirubinaemia can be caused by:
1) Increase production of Bilirubin.
2) Impaired metabolism
3) Decreased excretion. or
4) Combination of the above causes.

Major cause of Jaundice:
1) prehepatic:
   A) Haemolysis.
   b) Ineffective erythropoieses.
2) hepatic: pre. Microsomal: drugs e.g. Rifampicin which interferes with the Bilirubin uptake.

Microsomal: pematurity; vital hepatitis, Gilbert’s syndrome, najjar syndrome.

Post. Microsomal: impaired excretion; hepatitis, drugs, Intra hepatic obstruction, hepatitis, cirrhosis, lymphoma, tumors...etc.

3) post hepatic: Gall stones; biliary stricture; carcinoma of the pancreas or biliary tract or cholangitis.
Biochemical Assessment of liver function.

S – Bilirubin

1) Haemotylic jaundice :-
   T.S. Bilirubin is high especially the uncojugated form.
   Enzymes :-
   S. GOT ↑
   S. GPT SLIGHTLY ↑
   Urine urobilinogen is in the urine i.e. Bile pigment positive while Bile salt negative.

In Crigle – Najjar syndrome ; the unconjugated form of Bilirubin is highly increased (the free form).
Conjugated hyper – bilirubinaemia
This condition is result due to a leakage of Bilirubin from either hepatocytes or the biliary system in to the blood stream. The water soluble (the conjugated form), enters the systemic circulation then excreted into the urine to a deep orange – brown color (tea – color).

Here; Bile salt positive
While, Bile pigment Negative

Plasma Enzymes
The enzymes are used in the assessment of liver function are: s. Got &s. Gpt .to gather with s. Alkaline phosphatase & 8-glutammy transferase (GGT).
Here; S. Gpt & S. Alk. phosphatase are more specific for liver diseases. Increase in S. Got & S. Gpt reflect cell damage; in this case, S. levels of the enzymes increase 20 times than the normal range in hepatitis. While in obstructive jaundice: S. Alk. phosphatase increase 10 times than the normal range. 8–glutamyl transferase (GGT), is also increase in liver disease. Therefore, s. levels of the enzymes are very useful in following up the progress of liver diseases. Prothrombin time is also affected in liver disease; as the activity of vit. K-dependent clotting factors are synthesized by the liver. (factor VII).
An increase in the prothrombin Time is often an early feature of acute liver diseases.

**Plasma proteins:**
Protein is synthesized in the liver, so its conc. in the plasma reflect the functional capacity of the liver. Its value decreases in chronic liver disease, but it is usually normal in the early stages of a cute hepatitis.

In plasma immunoglobulin conc. may be noticed in alcoholic liver disease. IGA, IgG in acute hepatitis & IgM in primary biliary cirrhosis. Therefore, plasma proteins are of diagnostic value in the liver diseases.
In severe cases, hepatic failure may develop, but most patients eventually recover completely. S.GOT & S.G PT increase then return to normal after recovery within 20–30 days. While in cases with hepatits B & C Viruses, the enzymes remain elevated. Infection with hepatitis A never leads to chronic disease.

**chronic hepatitis:**
It is a hepatic inflammation remain for more than six months. There are many causes, e.g. Autoimmune hepatitis, chronic infection with hepatitis B or C & alcohol.
Auto immune typically occurs in young women although it can occur in either cases. Plasma Got & Gpt are usually elevated.

**A cute liver failure:**
It is a state of severe liver dysfunction. It can be hyper acute developing within seven days of the onset of jaundice. It is a rare condition. Toxin & hepatitis are the most frequent causes. Acute liver failure is often accompanied by renal failure. It is represented with hyponatraemia, hypocacimia and hypoglycemia. Lactic acid acidosis may develop as a result of failure of hepatic gluconeogenesis from lactate.
Alumina in chronic liver disease

8-globulin in cirrhosis, especially autoimmune diseases.

∞-antitrypsin in cirrhosis due to anti try sin deficiency.

∞-fetoprotein is highly in primary hepatocellular carcinoma.

Liver diseases

1- A cute hepatitis: it is usually caused by viral infection A, B, C, D, & E or by toxins e.g. alcohol, paracetamol, carbon tetra chloride (ccl4) or fungal toxins. Patients may represent with jaundice.

Bilirubin and urobilinogen are usually detectable in
urine. At the same time s. level of Bilirrubin is also increase.

Cirrhosis:
Causes of cirrhosis include chromic excessive alcohol in take; auto immune diseases e.g. auto immune hepatitis, primary biliary cirrhosis persistence B or C virus and various inherited metabolic diseases, such as Wilsons disease ....etc. metabolic and clinical abnormalities may occur later on. causes of death include uncontrolled bleeding .. spaticaemia . Long prothrombin time . and
elevated level of s. bilirubin are detected.

**Tumours and infiltrations:**
The liver is a common site for tumour metastasis. Primary tumours are associated with cirrhosis, hepatitis B & C and various carcinogens. Plasma α-fetoprotein is elevated.

Infiltrative conditions which can affect the liver include lymphomas and amyloidosis. Patients with such conditions and with intrahepatic tumours are often not jaundiced. The
only biochemical abnormality may be an increase in plasma Alkaline phosphatase activity.

**Inherited abnormalities of Bilirubin metabolism**

There are four conditions in which jaundice is caused by inherited abnormality of Bilirubin metabolism. Gilberts, Crigler–Najjar, Dubin–Johnson & Rotor syndromes. Gilberts syndrome affects 2-3% of the population but the others are rare. The jaundice of Gilberts syndrome is typically mild & present only
intermittently. It is often noticed after an infection or a period of deceased of food intake. The liver is histologically normal.
<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Defect Description</th>
<th>Clinical Features</th>
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<tbody>
<tr>
<td>Gilberts</td>
<td>Decreased conjugation</td>
<td>Mild or increase the unconjugated bili.</td>
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<tr>
<td>Crigler-Najjar</td>
<td>a) Absence of conjugating enzyme b) Partial defect.</td>
<td>Increase the free form.</td>
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<tr>
<td>Dubin-Johnson</td>
<td>Decreased hepatic excretion of Bili.</td>
<td>Mild hyperbilirubinemia, hepatic pigment disposition (melanim), bilirubinuria.</td>
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<tr>
<td>Rotor</td>
<td>Unknown</td>
<td>Similar to Dubin but not pigmentation.</td>
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uncommon liver diseases:

Wilsons disease is an Inherited abnormality of copper metabolism. characterized by decreased biliary excretion of copper. Copper is deposited in the liver. patients with Wilsons diseases may present either in child hood with hepatitis accompanied in many cases by haemolysis & renal tubular defect or in young with cirrhosis.

The biochemical features of Wilsons disease are a decreased in plasma cerulo plasmin conc. A low plasma copper & renal excretion of copper.

Gallstones
Consist mainly of chol. , calcium; salts and bilirubin. Gall stones may be
silent but it causes can biliary colic and obstruction. Biochemical tests may be of value in the management of such cases. S.Alk. phosphatase increase

S GOT

SGPT Moderate increase.

T.S. Bilirubin - especially the conjugated form.