Markers of Liver Disease

- The enzymes used in assessment of liver disease may be divided into two groups:

(a) Those indicating hepatocellular damage and

(b) Those indicating cholestasis (obstruction)

Markers of liver dysfunction.

- Enzyme indicating Hepatic cell damage.
  - ALT
  - AST.

Enzyme Indicating Cholestasis (obstructive liver disease)

- ALP
- GGT
- NTP (5' nucleotidase)

- Enzymes
- **1. Alkaline phosphatase.**
  - catalyze hydrolysis of phosphate esters at alkaline pH (9-10)
  - Zn containing enzyme.
  - It is an ectoenzyme - asso: with membranes of liver, kidney, intestine, bone osteoblasts.
  - Normal serum level - 40 - 125 IU/L.
  - activated by Mg & Mn.

Increase in ALP:

- Moderately high (hepatic disease).
  - 2-3 times
    - → Injective
    - → alcoholic liver disease
    - → Carcinoma.
- very high ALP noticed in obstructive jaundice or hepatic carcinoma.
  - **Extrahepatic obstruction**
    - gall stones
    - carcinoma head of pancreas.
  - **Intrahepatic obstruction**
    - Viral hepatitis
    - drugs.

Drastically high ALP : (10-25 times of upper limit)
- noticed in bone disease.

- pagets
- Rickets
- osteoblastoma
- Metastatic carcinoma of bone.
- Hyperparathyroidism.

2. Gamma Glutamyl transferase (GGT).

- Normal serum value - 10-30 IU/L
- Clinically important as it is sensitive to duct alcohol abuse
- elevated levels seen in chronic alcoholism.
- In liver diseases, GGT levels increases like that of ALP
- very sensitive of biliary tract diseases.

3. Nucleotide phosphatase (NTP)

- 5' nucleotidase
- marker enzyme of plasma membrane.
- Nickel inhibits NTP
- Ectoenzyme
- Normal level : 2-10 IU/L

Enzyme Indicating hepatic cell damage.

(1) Alanine transaminase. (ALT)

- serum glutamate pyruvate transaminase (SGPT).

- Normal level in Serum.

- males - 13-35 IU/L.
- females - 10-30 IU/L.

13-35
10-30

In liver diseases, ALT > AST.

- very high ALT (300-1000 IU/L).
  - acute hepatitis - toxic or viral.

- moderately high ALT (50-100 IU/L).
  - Chronic hepatitis.
  - cirrhosis
  - Hepatitis C
  - NASH (non alcoholic steatohepatitis)

2. AST.

- Normal 20 - 40 IU/L.

- AST is significantly elevated in liver disease.

✓ primary hepatoma

✓ alcoholic hepatitis.

Markers of prostate disease.

- PSA → prostate specific antigen.
- ACP → acid phosphatase.

(1) Prostate specific antigen (PSA)

- specific for prostate tissue.
- Normal value : 1 - 5 ug/L
- value above 10 mg/L indicative of prostate cancer.
- Bound and free forms present.
- 4 - 10 ug/L — Benign prostatic hypertrophy.
- >10 ug/L — Prostate cancer

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2) Acid phosphatase (ACP)

- Hydrolyze phosphoric acid ester.
- pH : 4-6 [acidic].
- site of secretion : prostate, RBC, WBC, platelets.
- Normal serum value - 2.5 - 12 IU/L.
- Elevated in bone metastasis of prostate cancer.
- Tumour marker [Increased in carcinoma].
- Blood for ACP should be collected before rectal examination.
- As prostate massage may increase the value.

Markers of Pancreatic Disease.

- Amylase.
- Lipase.

(1) AMYLASE.

- Serum amylase : 50 - 120 IU/L.
- produced by pancreas, salivary glands.

- Amylase; highly ↑ {1000 times}

- acute pancreatitis.
- Rises in 6-12 hours, lasts for 2-4 days.

Moderately ↑

- Chronic pancreatitis.
- mumps (parotitis).
- pancreatic duct obstruction.

50-120
50-175
2-14.

(2) LIPASE:

- 50-175 IU/L

- advantage over Amylase:
  - Elevated for 7-14 days
  - Not increased in mumps. {more specific}

- Highly increased. (upto 5 times)
  - Acute pancreatitis.

moderately ↑ Lipase.

- Carcinoma of pancreas
- Biliary disease.
- peptic ulcer

Enzyme profile in muscle disease.

- CK - MM
- aldolase (ALD) - earliest enzyme to rise.
- LDH
- AST - not specific.

CK-MM
aldolase
AST.
LDH.

Enzyme profile in bone disease.

- markers of osteoblast activity - ALP.
  increased in pagets, rickets, osteoblastoma.
- markers of osteoclast activity -
  TRAP - tartarate resistance acid phosphatase (db.)

Other enzyme patters in diseases.

- Cholinesterase - OP poisoning.
- G6PD - Drug induced hemolytic anemia.
- Ceruloplasmin - wilsons disease.
- Neuron specific enolase - Neuroendocrine tumours.

Enolase / Neuron specific enolase.

- Glycolytic enzyme.
- NSE is a tumour marker of for tumours of neuroendocrine origin.

{small cell lung cancer, neuroblastoma}.

Use of Enzymes.

- Therapeutic agents
- Diagnostic agents.

Therapeutic uses of enzyme.

1) streptokinase {from streptococci}
2) Urokinase. {from urine}.

} lyse intravascular clots in MI.

3) Asparaginase - anticancer drug.

4) pepsin
5) pancreatin {trypsin, lipase}.

} given to patients with dyslipidemia digestion

6) Streptokinase (DNAse) - applied locally.

7) papain - Anti Inflammatory.

8) α_1-antitrypsin - AAT deficiency / emphysema.

Enzymes as diagnostic agents.

- Enzymes are useful in clinical lab to estimate blood analytes.

1) Glucose oxidase - glucose.
2) urease - urea.
3) uricase - uric acid.
4) Hexokinase - glucose.
5) Cholesterol oxidase - cholesterol.
6) lipase - triglyceride.
7) peroxidase - Glucose, cholesterol.
8) Horse radish peroxidase } ELISA
   Alkaline phosphatase
9) restriction endonuclease - RFLP, southern blotting
10) Reverse transcriptase - PCR (RT-PCR).