Clinical Enzymology

Plasma enzymes

Blood plasma contains many enzymes, which are classified into functional and non-functional enzymes:

Functional enzymes present at all times in the circulation and perform a physiologic function in the blood, examples of these functional enzymes include lipoprotein lipase, pseudocholinesterase, and enzymes of blood coagulation. These enzymes are synthesized and secreted by the liver.

Non functional enzymes: plasma also contains numerous other enzymes that perform unknown physiologic function in blood. These non functional plasma enzymes arise from the routine normal destruction of erythrocytes, leukocytes, and other cells. Tissue damage or necrosis resulting from injury or disease is generally accompanied by increasing in the levels of several non functional plasma enzymes. Therefore several enzymes are used in the diagnosis.

Medical importance of non functional plasma enzymes.

Measurement of non functional enzymes is important for:
1. Diagnosis of diseases as diseases of different organs cause elevation of different plasma enzymes.
2. Prognosis of the diseases: we can follow up the effect of treatment by measuring plasma enzymes before and after treatment.
<table>
<thead>
<tr>
<th></th>
<th>Functional plasma enzymes</th>
<th>Non Functional plasma enzymes</th>
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</thead>
<tbody>
<tr>
<td><strong>Concentration in plasma enzymes</strong></td>
<td>Present in plasma in higher concentration in comparison to tissues</td>
<td>Normally, present in plasma in very low concentrations in comparison to tissues</td>
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<tr>
<td><strong>Function</strong></td>
<td>Have known functions</td>
<td>No known functions</td>
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<tr>
<td><strong>Substrate</strong></td>
<td>Their substrates are always present in the blood.</td>
<td>Their substrate are absent from the blood.</td>
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<td><strong>Site of synthesis</strong></td>
<td>Liver</td>
<td>Different organs e.g. liver, heart, brain, and skeletal muscles</td>
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<tr>
<td><strong>Effect of diseases</strong></td>
<td>Decrease in liver diseases</td>
<td>Different enzymes increase in different organ diseases</td>
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<td><strong>Examples</strong></td>
<td>Clotting factors e.g. prothrombin, lipoprotein lipase, and pseudocholine esterase.</td>
<td>ALT, AST, CK, LDH, alkaline phosphatase, acid phosphatase, and amylase.</td>
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Lactate Dehydrogenase (LDH) (LD)

1 – Normal values

Lactate dehydrogenase will convert pyruvate to lactate. The normal value of LDH in serum is 100 – 200 U/L. Values in upper range are generally seen in children. Strenuous exercise will slightly increase the value. LDH level is 100 times more inside the RBC than in plasma, and therefore minor amount of hemolysis will result in a false positive test.

2 – LDH and heart attack

In myocardial infarction, total LDH activity is increased. The time course of LDH level after a heart attack is given in the following figure. The magnitude of the peak value as well as the area under the graph will be roughly proportional to the size of myocardial infarction.

Creatine kinase (CK)

1 – Normal values

It is used to convert creatine to creatine phosphate, therefore it was called creatine phosphokinase in old literature. Normal serum value for CK is 15 – 100 U/L for males and 10 – 80 U/L for females.

2 – CK and heart attack

- CK values in serum is increased in myocardial infarction, the time course is shown in the former figure. The CK level starts to rise within 3 – 6 hours of infarction.
- Therefore CK estimation is very useful to detect early cases, where ECG changes is ambiguous.
- The CK level is not increased in hemolysis or in congestive cardiac failure, and therefore CK has an advantage over LDH. The area
under the peak and slope of initial rise are proportional to the rise of infarction.

3 – CK and muscle diseases
- The level of CK in serum is very much elevated in muscular dystrophies (500 – 1500 IU/L)
- CK level is highly elevated in crush injury, fracture and acute cerebrovascular accidents.

**Aspartate amino transferase (AST)**

- In old literature it was called as serum glutamate oxaloacetate transaminase (SGOT). AST needs pyridoxal phosphate (vit. B6) as coenzyme.
- Normal serum level of AST is 8 – 20 U/L. The level is significantly elevated in myocardial infarction. The time course of AST is shown in the former figure.
- It is moderately elevated in liver diseases.

**Alanine amino transferase (ALT)**

- In old literature it was called as serum glutamate pyruvate transaminase (SGPT). The enzyme needs pyridoxal phosphate as coenzyme.
- Normal serum level of ALT for male is 13 – 35 U/L. Very high values (300 – 1000 U/L) in acute hepatitis, either toxic or viral in origin.
- Both ALT and AST levels are increased in liver diseases, but ALT > AST.
**Alkaline phosphatase (ALP)**

- This enzyme is produced by osteoblasts of bone, and is associated with the calcification process. It is activated by magnesium and manganese. Zinc is a constituent ion of ALP.
- Normal serum value of ALP is 40 – 125 U/L. In children, the upper level of normal value may be more, because of the increased osteoblastic activity in children.
- Moderate increase (2-3 times) in ALP level is seen in hepatic diseases such as infective hepatitis, alcoholic hepatitis or hepatocellular carcinoma.
- Very high level (10 – 12 times of upper limit) may be noticed in extrahepatic obstruction (obstructive jaundice) caused by gallstone or by pressure on bile duct by carcinoma of head of pancreas.
- ALP is produced by epithelial cells of biliary canaliculi and obstruction of bile with consequent irritation of epithelial cells leads to secretion of ALP into serum.
- Drastically high levels of ALP (10 – 25 times of upper limit) are seen also in bone diseases where osteoblastic activity is enhanced such as Paget's disease, rickets osteomalacia, osteoblastoma, metastatic carcinoma of bone and hyperparathyroidism.

**Nucleotide phosphate (NTP)**

- It is also known as 5 nucleotidase, this enzyme hydrolyses 5 nucleotides to corresponding nucleosides at an optimum pH of 7.5. Nickel ions inhibit NTP.
- Normal NTP level in serum is 2 – 10 IU/L. It is moderately elevated in hepatitis and highly elevated in biliary obstruction.
Gamma Glutamyl Transferase (GGT)

- In the body it is used in the synthesis of glutathione. It is seen in liver, kidney, pancreas, intestinal cells and prostate gland.
- Normal serum value of GGT is 10 – 30 U/L. It is moderately increased in infective hepatitis and prostate cancer.
- GGT is clinically important because of its sensitivity to detect alcohol abuse. GGT is increased in alcoholics even where other liver function tests are within normal limits.
- GGT level is rapidly decreased within a few days when the person stops to take alcohol. Increase in GGT level is generally proportional to the amount of alcohol intake.

Enzyme Profile in Liver Diseases.

Enzymes commonly studied for diagnosis of liver diseases are:

1. ALT
2. ALP
3. NTP
4. GGT

Acid Phosphatase (ACP)

- Normal serum value of ACP is 2.5 – 12 U/L.
- ACP is secreted by prostate cells, RBC, platelets and WBC.
- ACP total value is increased in prostate cancer and highly elevated in bone metastasis of prostate cancer.
- ACP is an important tumor marker.
- Since blood cells contain excess quantity of ACP, care must be taken to prevent hemolysis while taking blood from the patient. Prostate massage may also increase the value. So blood may be collected for ACP estimation before rectal examination of patient.
Amylase

- This splits starch to maltose. It is activated by calcium and chloride ions. It is produced by pancreas and salivary glands.
- Normal serum value is 50 – 120 IU/L the value is increased 1000 times in acute pancreatitis which is a life threatening conditions. The peak values are seen between 5 – 12 hours after the onset of disease and returns to normal levels within 2 – 4 days after the acute phase.
- Moderate increase in serum levels are seen in chronic pancreatitis, mumps (parotitis) and obstruction of pancreatic duct.

Lipase

- It will hydrolyse triglycerides to beta monoglyceride and fatty acid. The enzyme is present in the pancreatic secretion.
- The level in blood is highly elevated in acute pancreatitis and this persists for 7 – 14 days. Thus lipase remains elevated longer than amylase.
- Moreover, lipase is not increased in mumps. Therefore, lipase estimation has advantage over amylase. It is moderately increased in carcinoma of pancreas, biliary diseases, perforating peptic ulcer.