Biochemistry Module For Medical Students
Discussion : Clinical Enzymology

Presented by:
A.P.Dr. Tahrir Etihad Kadium
(Ph.D. Clinical biochemistry).

Learning Objectives:

- **Understand the value of enzyme and isoenzymes in diagnosis**
- **Identify the sources of plasma enzymes and possible mechanisms responsible for abnormal levels**
- **List and study various enzymes that are used in diagnosis**

Clinical Enzymology

- **Enzymes can be measured in body fluids, mainly plasma, to aid the clinical diagnosis and management of certain conditions. This is called clinical enzymology.**

PLASMA ENZYMES:

➢ Enzymes present in plasma can be classified into **2 types**, they are

- Functional Plasma enzymes and
- Non-functional plasma enzymes

1. Plasma-derived enzymes (functional plasma enzymes):

- They are normally occurring functional plasma enzymes.
- Mostly synthesized by the liver.
- Their field of activity is plasma components and their activity are higher in plasma than in cells, e.g., coagulation enzymes.
- Their clinical importance is limited to diseases related to their own synthesis and function; i.e., abnormalities of metabolism of plasma lipoproteins and blood clotting, and the organ function of their synthesizing tissues, e.g., thromboplastin as a liver function test.

Cell-Derived enzymes (Non-functional plasma enzymes):

- Normally they locate to intracellular compartments; i.e., they are non -functional plasma enzymes.
- A very low plasma level normally.
- Gross damage to the cells or abnormal membrane permeability, overproduction of the enzymes or abnormal high cellular proliferation may allow their leakage in abnormally high amount into plasma and other body fluids.
- The amount and nature of the plasma enzyme(s) reflects the extent and nature of the damaged tissue.
- Measurement of these enzymes in plasma can be used to assess cell damage and proliferation i.e. diagnosis of disease.

- **INCREASED activity of non-functional** plasma enzymes could be due to increased release and/or impaired clearance.
- **DECREASED activity of non-functional** plasma enzymes could be due to decreased enzyme synthesis, increased enzyme inhibition and/or deficiency of its activating factors.

The enzyme activity in plasma may be:

- higher than normal, due to the proliferation of cells, an increase in the rate of cell turnover or damage or in enzyme synthesis (induction), or to reduced clearance from plasma.

- lower than normal, due to reduced synthesis, congenital deficiency or the presence of inherited variants of relatively low biological activity.

- Clinical enzymology has limitations, as plasma enzyme activity lacks specificity. Isoenzyme determination or measuring a number of enzymes may increase diagnostic accuracy.

The diagnostic precision of plasma enzyme analysis may be improved by the following:

- **Serial enzyme estimations:**

  A persistently raised plasma enzyme activity is suggestive of a chronic disorder or, occasionally, impaired clearance.

- **Isoenzyme determination:**

  Some enzymes exist in more than one form; these isoenzymes may be separated by their different physical or chemical properties. If they originate in different tissues, such identification will give more information than the measurement of plasma total enzyme activity; Examples are ALP (hepatic, bone, intestinal and placental isoenzymes) and CK (striated muscle, MM; brain, BB; and cardiac muscle, MB).

- **Estimation of more than one enzyme:**

  Many enzymes are widely distributed, but their relative concentrations may vary in different tissues. For example, although both ALT and AST are abundant in the liver, the concentration of AST is much greater than that of ALT in heart muscle.

Enzymes in Diagnosis and Prognosis:

- **Enzyme activity is expressed in International unit (IU)**

It corresponds to the amount of enzymes that catalyzes the conversion of one micromole (μmol) of substrate to product per minute (μmol/min).

- Plasma enzyme activities can be used in the diagnosis of disease and prognosis of treatment. The disease process may cause changes in the cell membrane permeability and release the intracellular enzymes into the plasma. The circulating enzymes can be quantified by measuring their catalytic activity or kinetic properties.
- Assays of enzymes in blood are useful for diagnosis of some diseases: amylase and lipase in pancreatitis, alanine transaminase in hepatitis, aspartate transaminase, lactate dehydrogenase and creatine phosphokinase in myocardial infarction, etc. These diseases involve death of the affected tissue, with release of the cellular contents into the blood.
- Clinical enzymology is a useful diagnostic tool, and several enzymes are estimated routinely in most clinical laboratories .Some of the most important ones are:

Enzymes routinely measured

NAME OF THE ENZYME	PRESENT IN
Aspartate Amino transferase (AST) Serum glutamate-oxaloacetate transaminase (SGOT)	Heart and Liver
Alanine Amino transferase (ALT) Serum glutamate-pyruvate transaminase (SGPT)	Heart and Liver
Alkaline Phosphatase (ALP)	Bone, intestine and other tissues
Acid Phosphatase (ACP)	Prostate
γ glutamyl Transferase (γ GT)	Liver
Creatine kinase (CK)	Muscle Including cardiac muscle
Lactate Dehydrogenase (LDH)	Heart, liver, muscle, RBC
α Amylase	Pancreas

Table : Commonly assayed enzymes for specific diagnosis:	
Aspartate transaminase (AST) (formerly known as *glutamate oxaloacetate transaminase*, or **GOT**)	Rises in myocardial infarction after CK and returns to normal in 4–5 days. Early indicator of hepatocellular damage
Alanine transaminase (ALT) (formerly known as *glutamate pyruvate transaminase*, **GPT)**	Marked elevation in acute hepatitis (viral or toxic) and in other parenchymal liver disease
Alkaline phosphatase (ALP)	Marked elevation in obstructive liver disease and in bone diseases with increased osteoblastic activity, e.g. rickets.
Acid phosphatase (ACP)	Marker for carcinoma prostate. Rises in metastatic bone diseases, especially from primary prostate.
Lactate dehydrogenase (LDH)	Rises in myocardial infarctions after CK and AST; LDH_1 becomes more than LDH_2 (called flipped pattern).
g-Glutamyl transpeptidase (GGT)	Liver disease, especially alcoholism.
Creatine kinase (CK)	Marked increase in muscle disease (CK-MM) and in myocardial infarction (CK-MB is the first enzyme to rise).
Amylase	About 1000-fold rise in acute pancreatitis
Lipase	Highly elevated in acute pancreatitis
Prostate specific Antigen (PSA)	Marker for prostate carcinoma
LDH_1 and LDH_2 *lactate dehydrogenase* isoenzymes 1 and 2.	

Summary:

- Enzymes can be measured in body fluids, mainly plasma, to aid the clinical diagnosis and management of certain conditions. This is called clinical enzymology.
- Enzymes may exist as isoenzymes, which may be present in different tissues. Examples are ALP (hepatic, bone, intestinal and placental isoenzymes) and CK (striated muscle, MM; brain, BB; and cardiac muscle, MB).
- Clinical enzymology has limitations, as generally plasma enzyme activity lacks specificity. Isoenzyme determination or measuring a number of enzymes may increase diagnostic accuracy.

- Note: the information in the two tables are important.