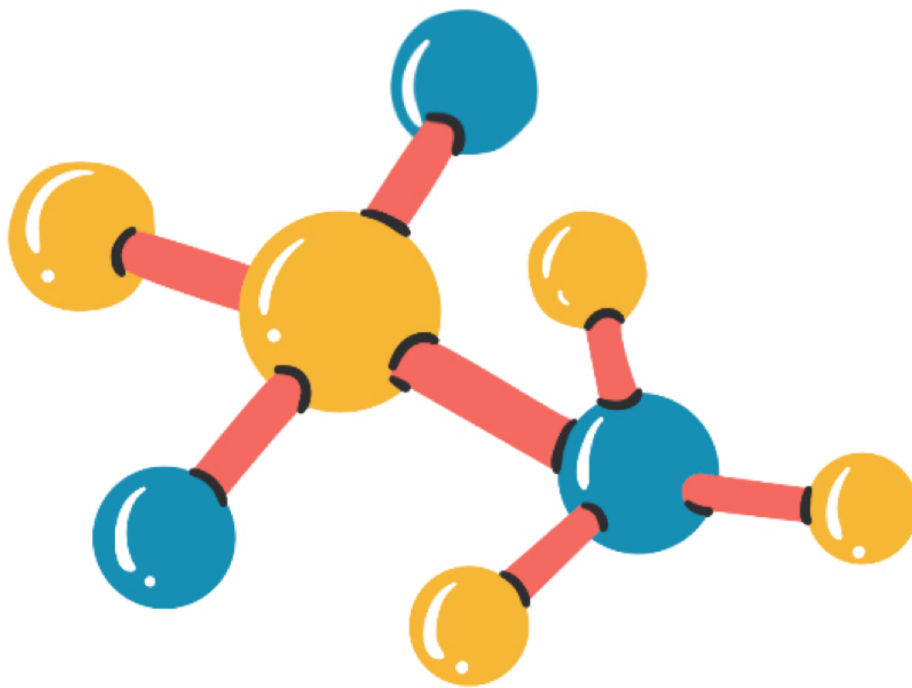


# Biochemistry



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## Enzymes in medical diagnosis:

What is the idea behind using the enzymes in medical diagnosis?

How can enzymes be used to diagnose diseases?

- If you have a blood sample and you quantify the amount of an enzyme that it has, this quantification will tell you if the owner of the blood sample has a disease or not.
- Explanation : as explained earlier isozymes existed to serve different means in different tissues that's why isozymes differ in the localisation, the idea is if you have a high concentration of a certain enzyme which is supposed to be in a certain tissue in a high concentration above normal limits in the blood this is due to the death of the tissue it serves as the cells are starting to die and opening up, all their contents are getting out which will be reflected to the extracellular space then reflected in the blood.

**High** concentration of a certain enzyme in the blood → the tissue of this enzyme is **dying** → A medical action interferes to save this tissue.

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- **Diagnostic enzymes :**

Ex: **ALT, AST, LDH, CK(CPK).**

**-Liver disease:** ALT & AST.

-Both localised in liver .

- **ALT** is very specific for the liver ( the most specific liver enzyme ) . It's a transaminase that converts pyruvate to Alanine and Alanine to pyruvate ( keto acid to amino acid — amino acid to keto acid ).
- **AST** ( Aspartate transaminase) converts aspartate to oxaloacetate and oxaloacetate to aspartate. Is present in higher concentration in the liver yet it is not exclusively restricted in the liver, it is present in the heart.
- **If a blood sample reads both ALT & AST in high concentrations what does that indicate?**
- It indicates a problem in the liver.

{ if only the AST is in high concentrations it indicates a probable issue in the heart or the liver.

### **How to diagnose whether it's in the heart or the liver?**

Symptoms, if the patient complains from chest pain → heart.

If it's abdominal pain → liver. }

- **AST** is more **sensitive** ( higher concentration, easily read in blood ) & **ALT** is more **specific** , compared to each other.
- The ratio can be diagnostic ( ALT/AST ).
  - Less than 1 : no viral origin .
  - Greater than 1: viral hepatitis, as viral cells affect the cells in a huge manner so all the tissue cells open up all together.

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- **Myocardial infarction:**

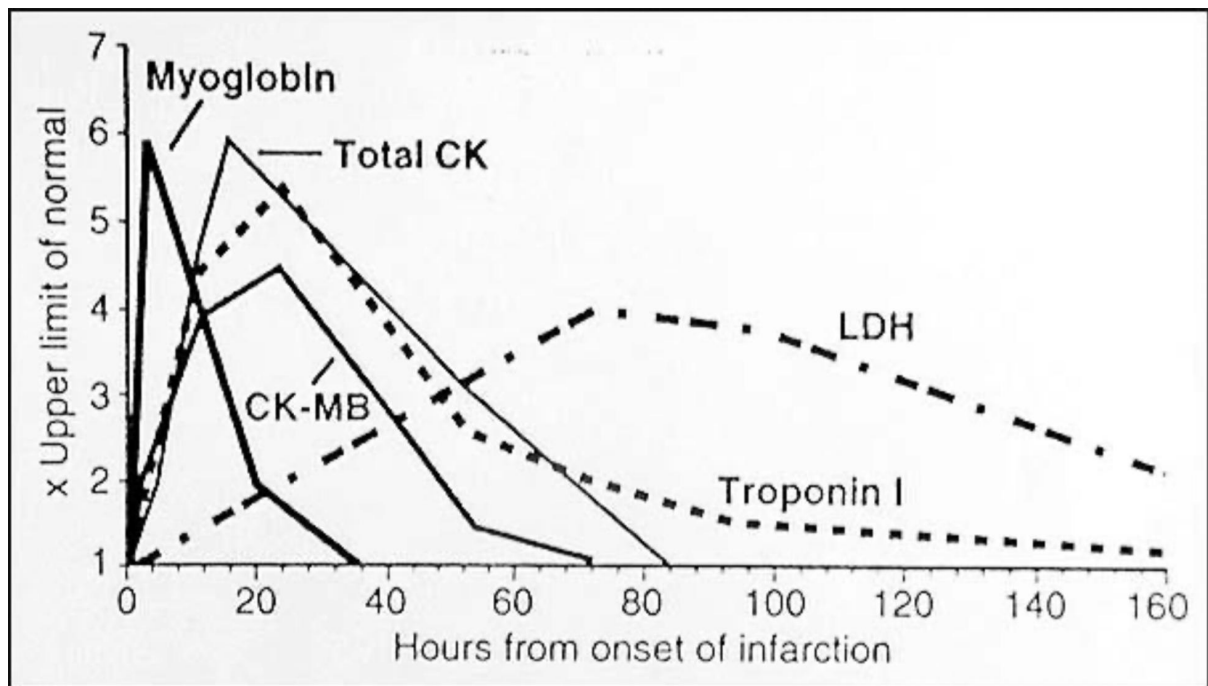
-Myo → muscle.

-cardial → with respect to the heart.

-infarction → the formation of a thrombi in the blood vessels - the blocking of an artery ( جلطة ) / ( خثرة ) .

1. The first step to take when a patient complains from chest pain is → ECG ,it tells if the patient has a myocardial infarction or not. However, a normal ECG doesn't exclude myocardial infarction as a potential cause of pain.
2. Another way to diagnose a myocardial infarction is by blood tests to check out two enzymes **LDH & CK**.

To talk further about these two enzymes, first check this Graph :



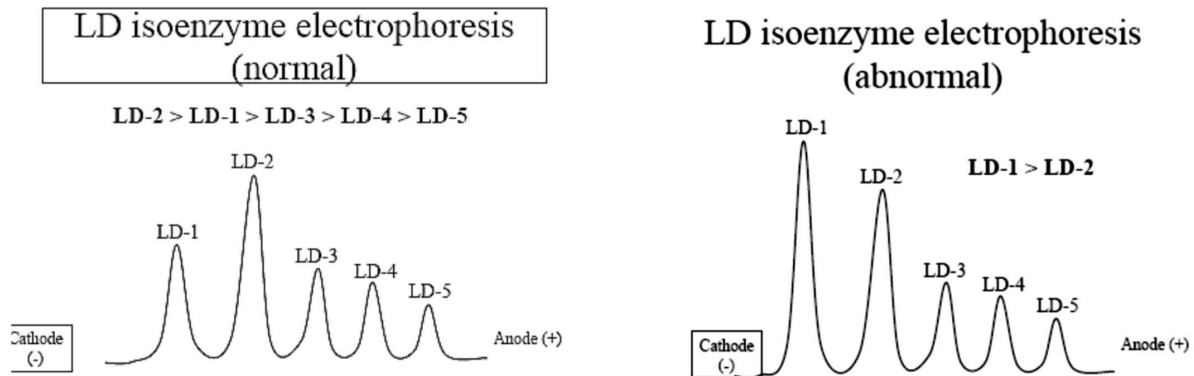
- The Y axis refers to how many folds of this enzyme are now in the blood compared to the normal level. In brief if an enzyme got 3 on the Y axis it means currently this enzyme has its concentration 3 times higher than the normal limit.
- The X axis indicates the time starting from the first sight of symptoms, meaning the patient did undergo the infarction.

### LDH:

-LDH gets its peak to 4 folds of the normal concentration approximately after three days around 70 hours. So if a patient complains of chest pain, within the first 3 days LDH is the one to check to diagnose an infarction. However, after the third day LDH concentration starts to decrease as a result LDH won't help much in the diagnosis .

- The increase of LDH generally in the blood in a myocardial infarction is due to the increase of LDH1 ( already explained in sheet 29).

This graph represents both LDH1&LDH2 concentrations in two conditions:



- LDH1 has a lower concentration than LDH2 in the blood so by running gel electrophoresis in a normal condition LDH1 will show up in a lesser degree than the LDH2. HOWEVER, in myocardial infarction this ratio will be flipped LDH1 concentration will be higher than LDH2 concentration .
- LDH-1/LDH-2 ratio is diagnostic for myocardial infarction (heart attacks).
- Normally, this ratio is less than 1.
- Following an acute myocardial infarct, the LDH ratio will be more than 1.

### CK:

-It's a dimer formed of **two** subunits and has **three** isozymes.

-The two subunits are : M subunit & B subunit.

- B —> represents the Brain.
- M —> represents the skeletal muscles.

-A two B subunits Ck enzyme is localised in the brain & A two M subunits Ck enzyme is localised in the skeletal muscles.

-if a patient complains of unexplainable headaches and when you run blood tests for a specific isozyme & the test shows that Ck the bb type is higher in concentration than normal, as a result you are up to diagnose the patient with a potential brain cancer.

- if the Ck mm type is higher in concentration than normal you are expected to have a skeletal muscle tumor or cancer or maybe an injury to the skeletal muscles.

This graph indicates the location of these isozymes:

Serum	Skeletal Muscle	Cardiac Muscle	Brain
0 trace BB <6% MB >94% MM	0 trace BB 1% MB 99% MM	0% BB <b>20% MB</b> <b>80% MM</b>	97% BB 3% MB 0%MM

- Heart, skeletal muscles, & brain.
- Like LDH, there are tissue-specific isoenzymes of CPK:
  - CPK3 (CPK-MM): the predominant isozyme in muscle.
  - CPK2 (CPK-MB): accounts for ≈35% of CPK activity in cardiac muscle, but less than 5% in skeletal muscle.
  - CPK1 (CPK-BB) is the characteristic isozyme in the brain and is significant in smooth muscle.

[ The increase in the total CK concentration is primarily due to the increase of CK-MB, so total CK reaches around 6 folds of the normal level & CK-MB is responsible for 4.5 folds in increase ]

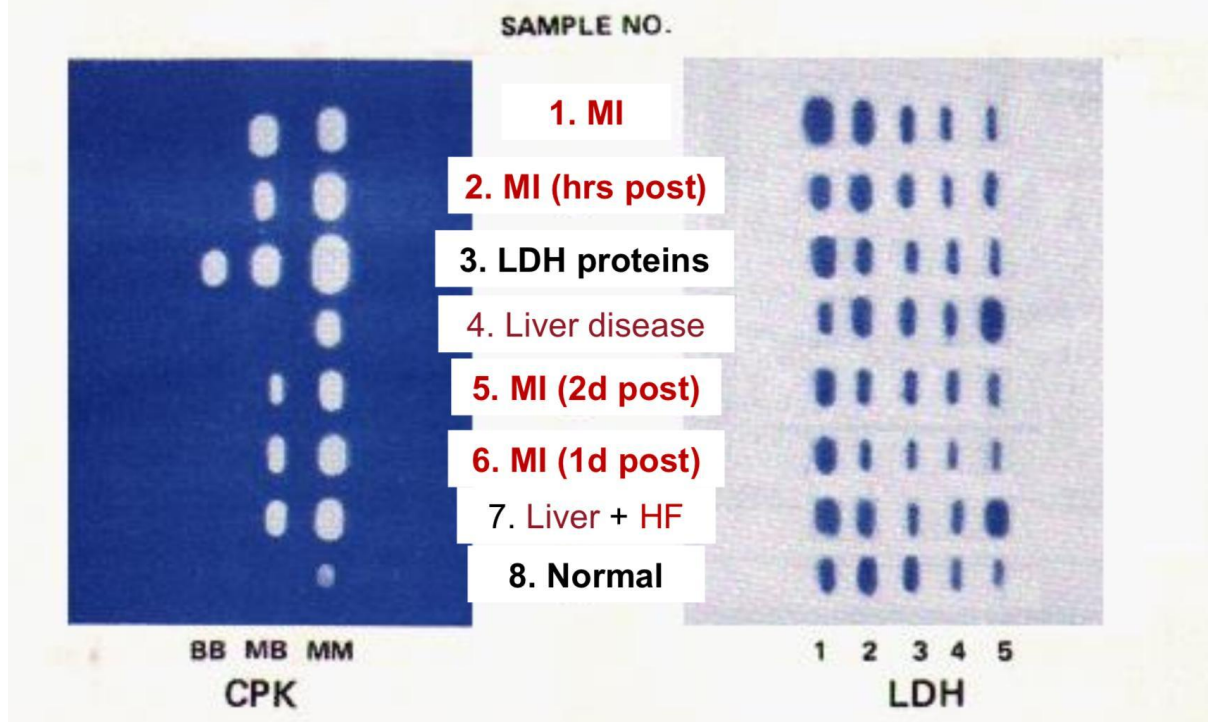
- This enzyme reaches its peak in the first day of infarction after 24 hours the level decreases losing its diagnostic importance.

**If you run a test for CK-MB and it's higher than the normal what would it be?**

- It would be another infarction as it's common for patients with infarctions.

This graph shows a comparison between LDH & CK :

## Correspondence Between CPK and LDH Isoenzyme Patterns



- + In gel electrophoresis, when bands get bigger it means a higher concentration of a specific protein & smaller ones are with lower concentration.
- + When two bands are next to each other yet one of them is bigger this means that the ratio is greater than 1 and so on .

### Explanation for the 8 samples :

**Sample #3** represents results for a control.

**Sample #8** results are from a normal specimen.

**Sample# 1** MI patient. The specimen was collected at a time when the activity of both LDH and CK were

elevated. Note the LDH flip and the high relative activity of the MB isoenzyme.

**Sample# 2** MI patients who experienced chest pain only several hours previously. Total CK is significantly elevated with a high relative MB isoenzyme activity.



**Sample# 6** MI patient (the 1st day post MI); CK activity is definitely elevated with a high relative MB isoenzyme activity and the LDH flip is evident.

**Sample# 5** MI patient (2 days post MI) so that CK has almost returned to normal activity and the LDH flip is definite.

**Sample# 7** MI patient with complications of heart failure and passive liver congestion or the patient was involved in an accident as a consequence of the MI, and suffered a crushing muscle injury.

**Sample# 4** a patient with liver disease. Although the LDH isoenzyme pattern is indistinguishable from muscle disease or injury, the absence of at least a trace of CK-MB isoenzyme is inconsistent with the muscle CPK isoenzyme distribution as is the apparently normal total activity.

## Troponins in MI

- Like all cardiac markers, troponins have a unique diagnostic window
- Troponin levels rise within four to six hours after the beginning of chest pain or heart damage, and stay elevated for at least one week.
- This long elevation allows detection of a myocardial infarction that occurred days earlier, but prevents detection of a second infarction if it occurred only days after the first

Good Luck