



# ENZYMES OF CLINICAL IMPORTANCE I

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Advance Clinical Biochemistry II (MA 406)

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Lecture Five

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# Objectives



- **At the end of this lesson, the students should be able to:**
- Understand the general concept of the clinical enzymology.
- Understand the enzymatic importance in clinical diagnosis.
- Understand the difference between functional and non-functional enzymes.
- Understand and note the factors affecting enzymatic activities

## Cellular Digestion and the Secretory Pathway

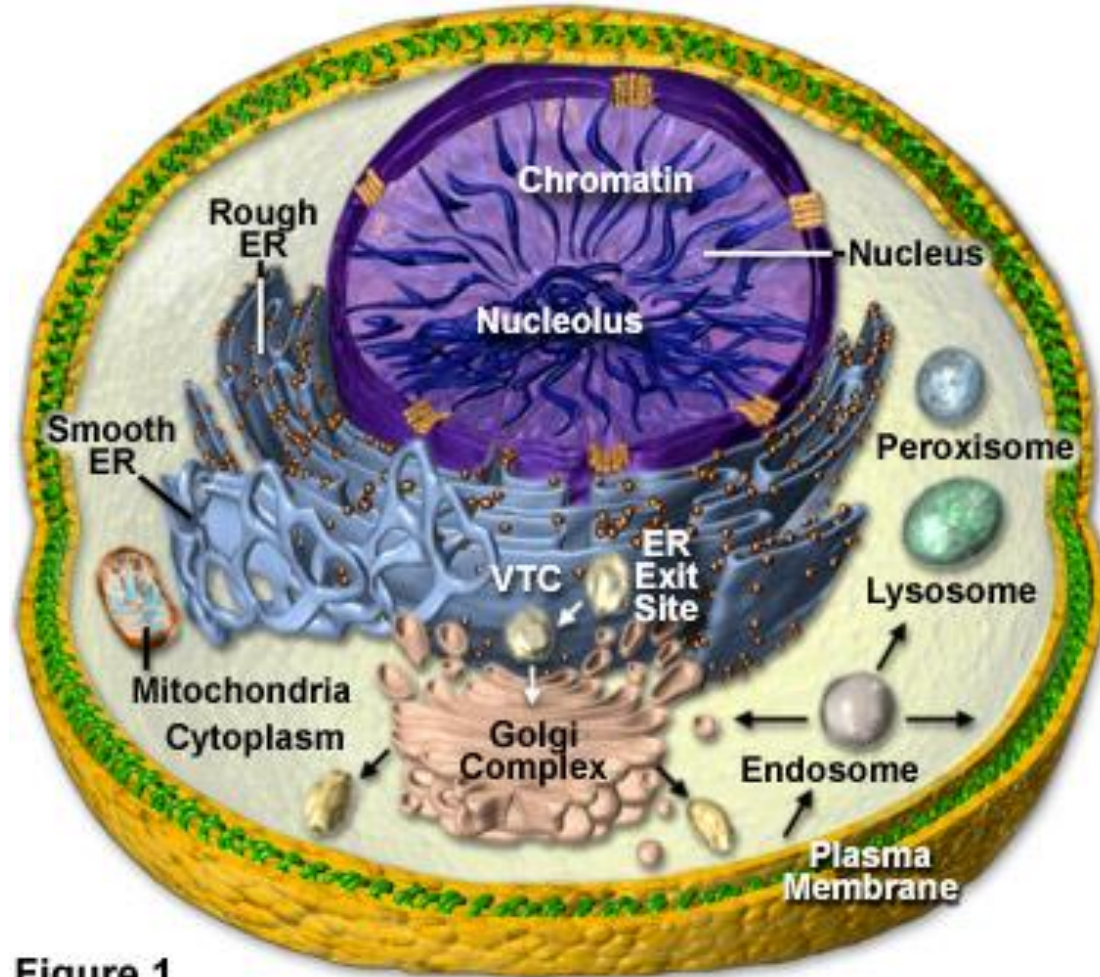


Figure 1

# Introduction

- Enzymes are protein catalysts that increase the rate or velocity of biological reactions in the body.
- In general, most enzymes are present in cells at much higher concentrations than in plasma.
- Measurement of their levels in plasma indicates whether their tissue of origin is damaged leading to the release of intracellular components into the blood.

# Clinical Enzymology

## Cont.

- Clinical enzymology is regarded as the measurement of enzyme activity for the diagnosis and treatment of diseases.
- Samples, usually blood, are taken from patients, as an aid to the diagnosis and understanding of disease.
- Both serum and plasma parts of blood could be used for the diagnosis involving enzymes.

# Types of plasma enzymes

## A. Enzymes that have definite physiological functions in circulation such as

- Lipoprotein lipase
- Proenzymes of blood coagulation

## B. Enzymes that reflect organ pathophysiology

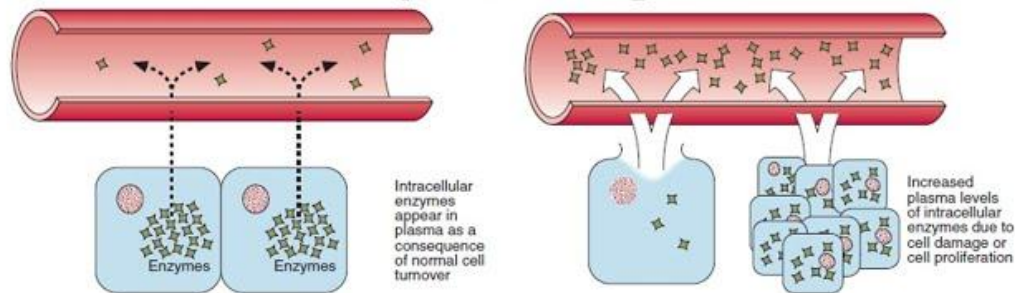
- Normally present in extremely low concentrations in plasma as compared with their high concentrations in various tissues.
- In case of tissue damage, they are released in greater amounts causing higher plasma levels which have diagnostic and sometimes prognostic significance.
- Include:
  - Enzymes present in exocrine secretions, which diffuse passively into the circulation e.g., amylase and lipase in pancreatic disorders.
  - Intracellular enzymes: enzymes used to detect pathological disorders of the various organs of the body e.g., myocardial infarction and hepatitis.

	enzymes	plasma enzymes
Concentration in plasma	Present in plasma in higher concentrations in comparison to tissues	Normally, present in plasma in very low concentrations in comparison to tissues
Function	Have known functions	No known functions
The substrates	Their substrates are always present in the blood	Their substrates are absent from the blood
Site of synthesis	Liver	Different organs e.g. liver, heart, brain and skeletal muscles
Effect of diseases	Decrease in liver diseases	Different enzymes increase in different organ diseases

## Sources of nonfunctional enzymes

- **Increase in the rate of enzyme synthesis** e.g., bilirubin increases the rate of synthesis of alkaline phosphatase in obstructive liver diseases.
- **Obstruction of normal pathway** e.g., obstruction of bile ducts increases alkaline phosphatase.
- **Increased permeability** of cell membrane as in tissue hypoxia.
- **Cell damage** with the release of its content of enzymes into the blood e.g., myocardial infarction and viral hepatitis.

### Clinical Biochemistry Plasma Enzymes in diagnosis

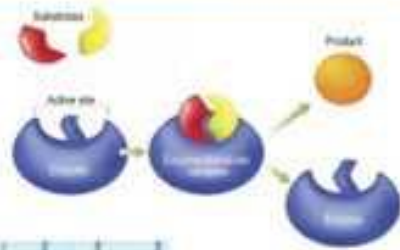


## Medical importance of NFPE

- Measurement of non-functional plasma enzymes for:
  1. **Diagnosis of diseases:** diseases of different organs cause elevation of different plasma enzymes.
  2. **Prognosis of the disease:** follow up the effect of treatment by measuring plasma enzymes before and after treatment.

### Clinical Enzymology

Enzymology



Clinical

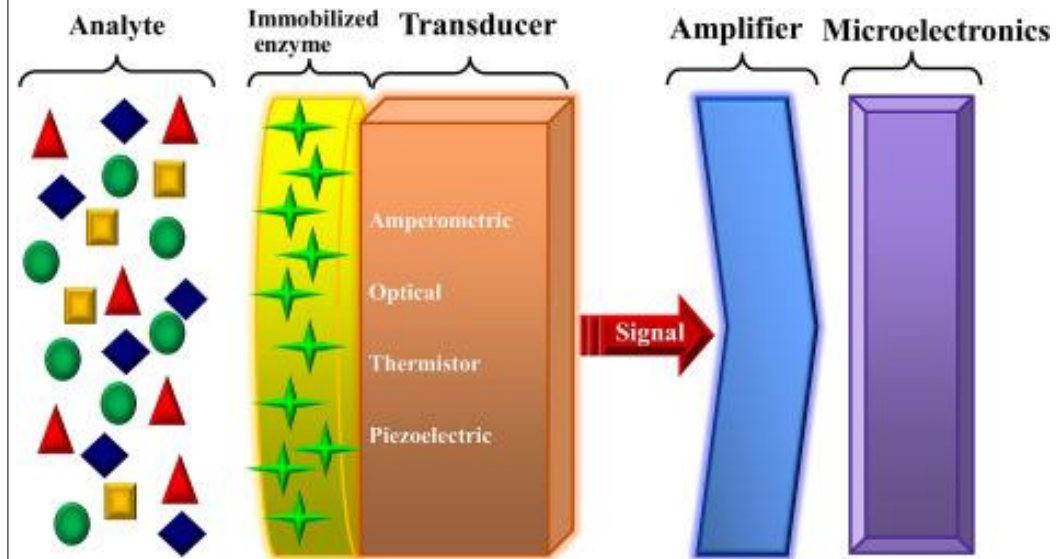




## Assessment of Cell Damage and Proliferation

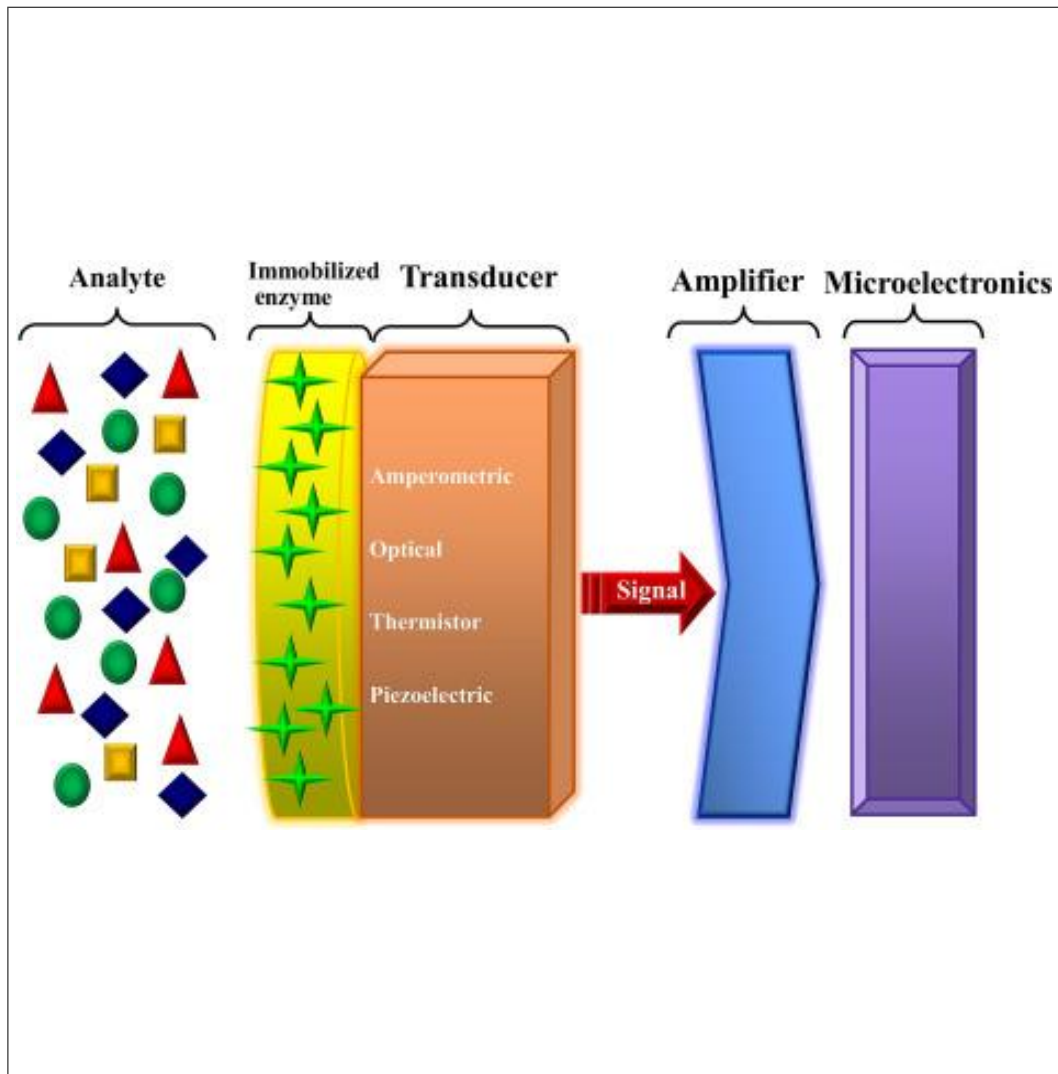
- Plasma enzyme levels depend on the extent of cell damage and the rate of release from damaged cells.
- Plasma enzyme levels depend on the balance between the rate of influx of active enzyme into the circulation and its eventual clearance from the blood.
- The rate of influx is determined by the rate of release from damaged cells and the altered rate of enzyme synthesis.

# The diagnostic precision of plasma enzyme analysis



## 1. 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 available in the liver, the concentration of AST (GOT) is much greater than that of ALT (GPT) in heart muscle.



**Cont.**

## 2. Serial enzyme estimations:

- The rate of change of plasma enzyme activity is related to a balance between the rate of entry and the rate of removal from the circulation.

## 3 Isoenzyme determination:

- Some enzymes exist in more than one form; these isoenzymes originate in different tissues.
- For example, CK may be derived from skeletal or cardiac muscle, but one of its isoenzymes is found predominantly in the myocardium

## Factors Affecting Enzymatic Activity



## Factors Affecting Results of Plasma

### Enzyme Assays

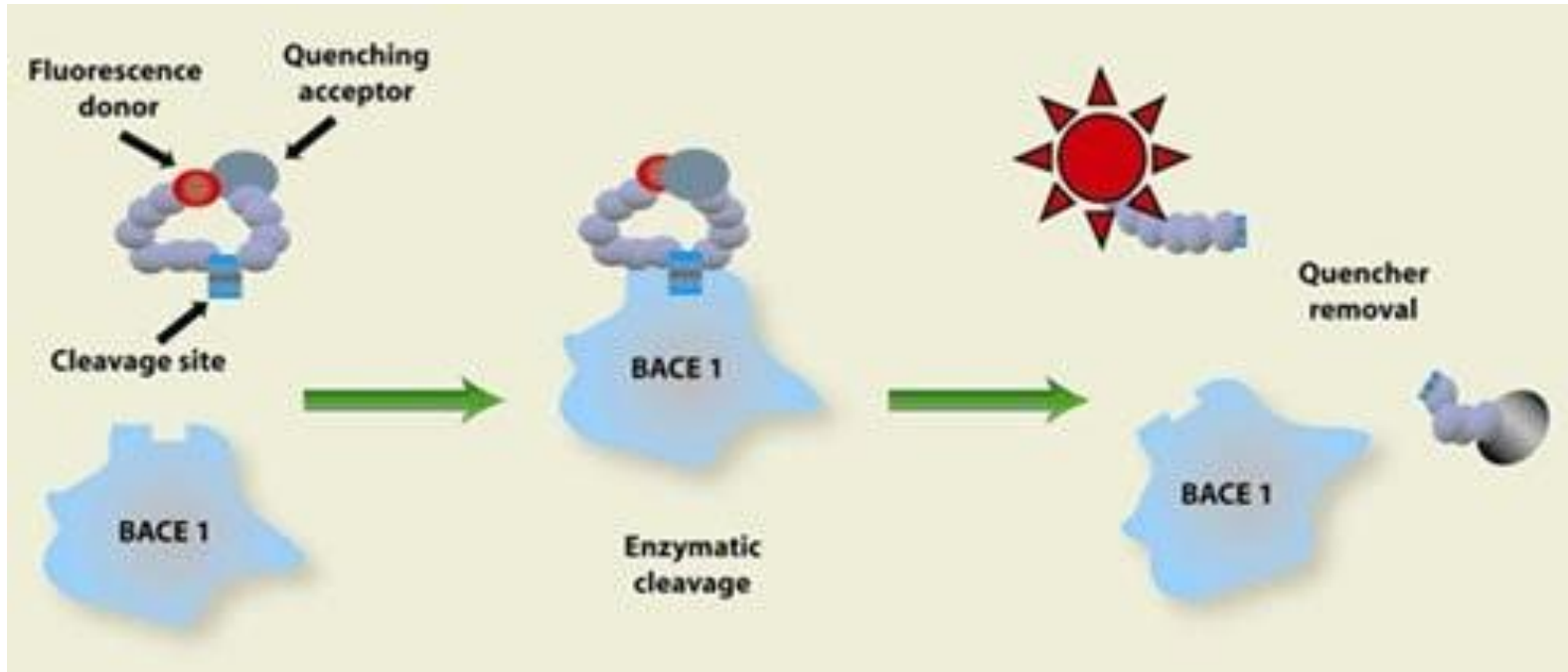
#### Analytical factors:

1. substrate concentration
2. product concentration
3. enzyme concentration
4. reaction temperature
5. reaction pH
6. presence of activators or inhibitors

## Cont.

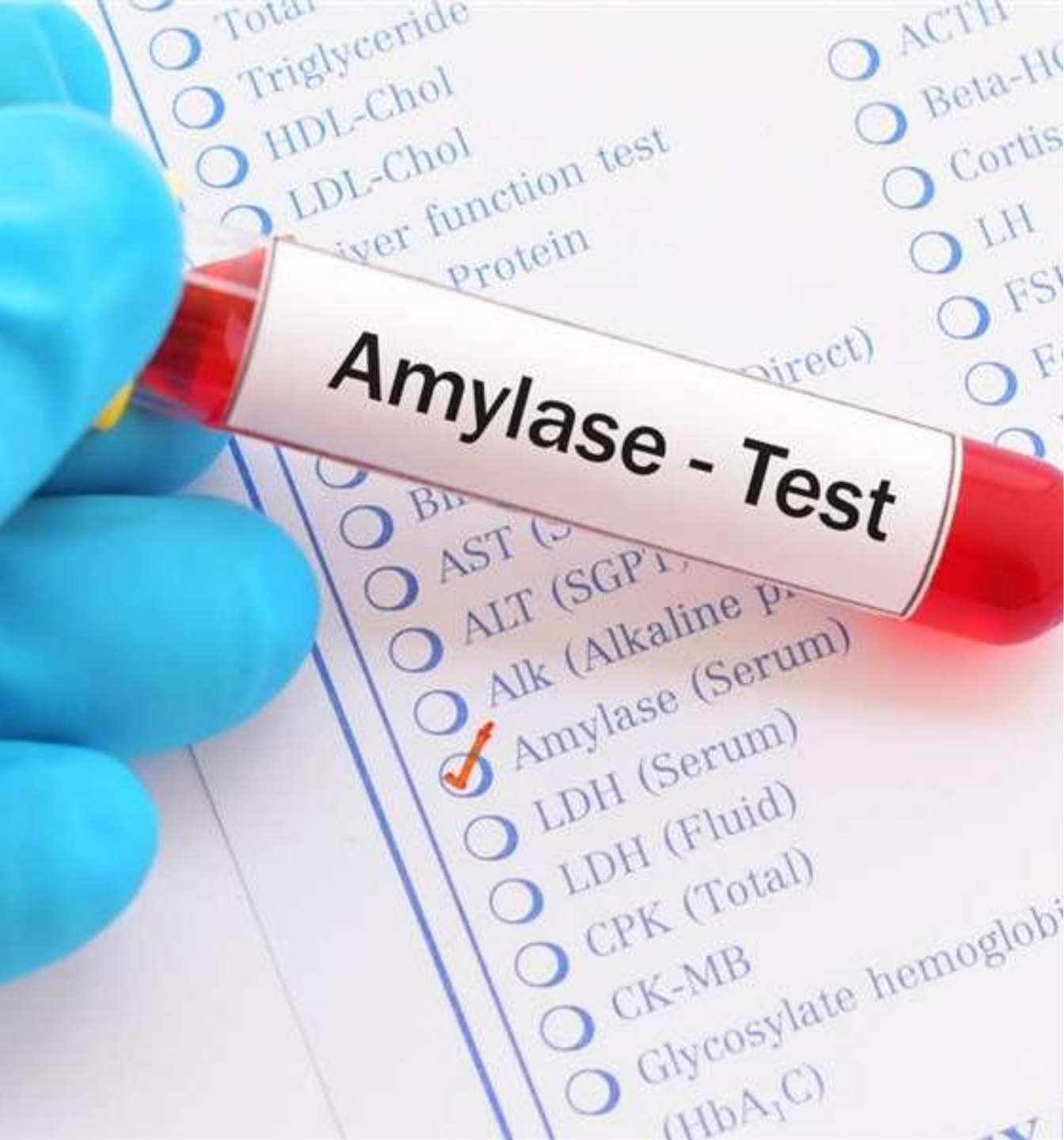
- Non-disease factors
- Age: period than in adults. Plasma ALP activity of bony origin is higher in children than in adults.
- Sex: Plasma GGT activity is higher in men than in women. Plasma CK activity is also higher in males.
- Race/ethnicity: Plasma CK activity is higher in black people than in white people.
- Physiological conditions: Plasma ALP activity rises during the last trimester of pregnancy, Why?
- Several enzymes, such as AST and CK, rise moderately in plasma during and immediately after labor or strenuous exercise.





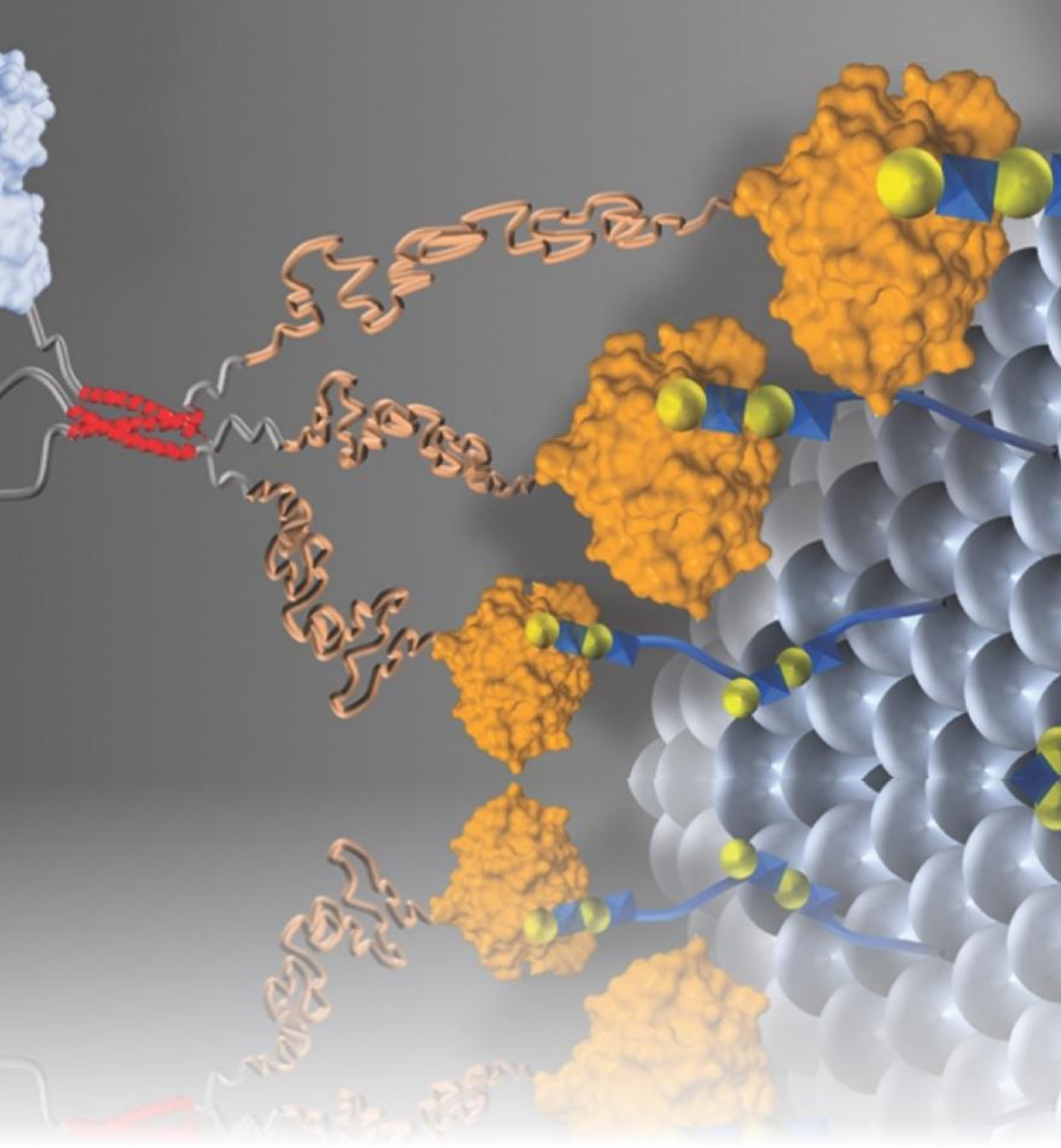
## Measurement of enzyme activity

- Enzyme activity is expressed in International unit (IU/L)
- It corresponds to the amount of enzymes that catalyze the conversion of one micromole of a substrate to product per minute per liter.



## Diagnostic Enzymes in Different Diseases

- Enzyme estimations are helpful in the diagnosis of
  - Liver diseases
  - Myocardial Infarction
  - Muscle diseases
  - Bone diseases
  - Cancers
  - GI Tract diseases



## Cont.

- **Liver enzymes**
  - Markers of hepatocellular damage.
  - Markers of cholestasis
- **Pancreatic enzymes**
  - Amylase
  - Lipase
  - Trypsin
- **Muscle enzymes**
  - Creatine Kinase
  - Lactate Dehydrogenase
  - Acid Phosphatase
  - Glucose -6-phosphate Dehydrogenase



# Detection of Enzymes for diagnosis of disease

Disorders	Enzymes
Liver Function Tests	SGOT, SGPT, ALP, GGT
Cardiac Function Tests	CK-MB, Troponins
Pancreatic Enzymes	Amylase, Lipase
Muscle Enzymes	CK, LDH

# Enzymes for Diagnosis of Liver Diseases

- **Markers of hepatocellular damage.:**
  - Enzymes that are normally present inside the hepatocytes are released into the blood when there is hepatocellular damage
    - **Alanine aminotransferase (ALT)**
    - **Aspartate aminotransferase (AST)**
- **Markers of cholestasis :**
  - Enzymes which are primary membrane membrane or side of hepatocytes)
    - **Alkaline phosphatase,**
    - **Gamma glutamyl transferase (GGT)**
    - **5-nucleotidase**

# Markers of hepatocellular damage

## ○ Aminotransferases/Transaminases

- The transaminases are enzymes involved in the transfer of an amino group from a **2-amino acid to a 2- keto acid**
- The aminotransferases are used as part of the **biochemical liver profile**.
- **Aminotransferases** are **sensitive indicators of liver cell injury** and are most helpful in recognizing acute hepatocellular diseases such as hepatitis.
- These enzymes are released into the blood in greater amounts when there is damage to the liver cell membrane resulting in increased permeability.



## Cont.

- **Types of plasma Aminotransferases:**
  - **Aspartate Aminotransferase (AST) enzyme** is also called serum glutamic oxaloacetic transaminase (SGOT).
  - **Alanine Aminotransferase (ALT) enzyme** is also called serum glutamic pyruvic transaminase (SGPT)

## ○ **Aminotransferases/Transaminases**

- **AST and ALT enzymes** are more important in assessing and monitoring the degree of liver cell inflammation and necrosis.
- **In acute viral hepatitis** there is a 100-1000 times increase in both ALT and AST but ALT level is increased more than that of AST.
- According to the AST/ALT ratio, we can estimate the extent of the liver damage.
- Elevated **plasma ALT** is relatively **specific for liver disease than AST** as AST may be elevated in other forms of tissue damage, such as myocardial infarction, muscle necrosis, and renal disorders.
- Aminotransferases levels **> 1000 IU/L** occur almost exclusively in disorders associated with extensive hepatocellular injury
- **Clinical Significance**
  - **Normal values of AST:** (Male: <35 U/L                      Female: <31 U/L)
  - **Normal values of ALT:** (Male: <45 U/L                      Female: <34 U/L)



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