

# Clinical applications of enzymes

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# Clinical application of enzymes

- ▶ **For the diagnosis of the disease**
  - **As therapeutic agents**
  - **As analytical reagents**

# Diagnostic Use of Enzymes



▶ marker of **cellular damage**

▶ The enzymes that are found in plasma can be categorized into two major groups:

**Plasma specific/functional** enzyme

These enzymes are clinically of interest when their concentration decreases in plasma

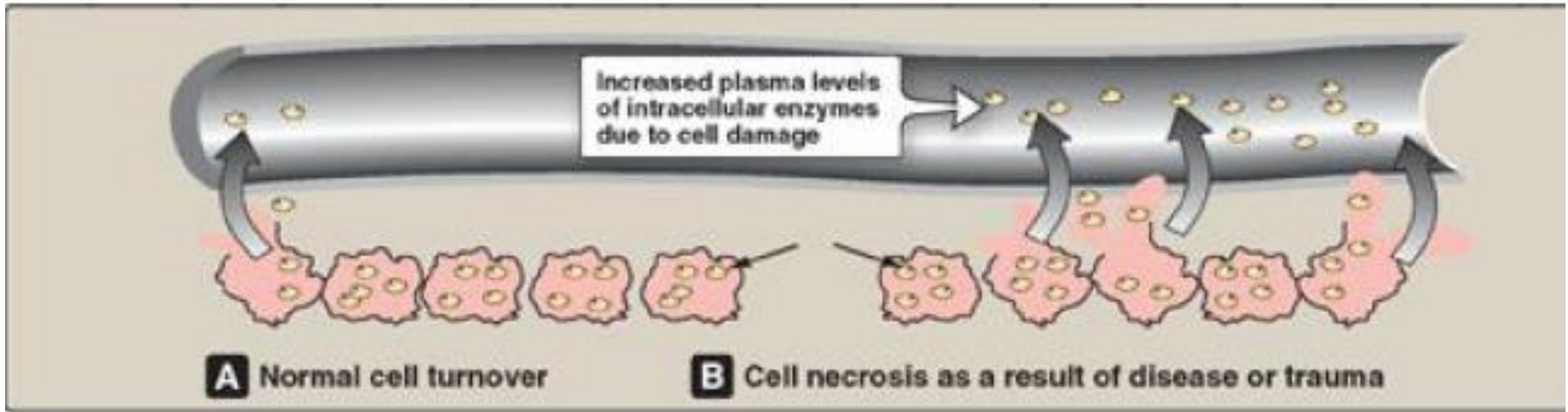
**Plasma nonspecific/ non-functional** enzyme.

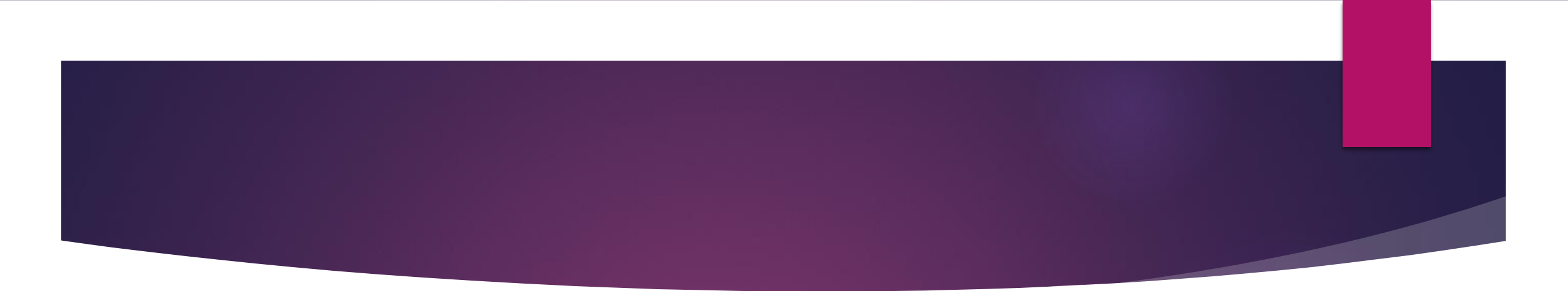
present in very high concentration in tissues than in the plasma.

Table 6:9: Enzymes of diagnostic importance

<i>Enzyme</i>	<i>Clinical Application</i>
Acid phosphatase	Prostatic cancer
Alanine aminotransferase	Liver disease (viral or toxic hepatitis), jaundice and liver cirrhosis
Aldolase	Muscle diseases
Alkaline phosphatase	Obstructive jaundice, bone diseases such as Paget's disease, rickets, osteomalacia, carcinoma of bone and hyperparathyroidism
Amylase	Acute pancreatitis, mumps, obstruction in pancreatic duct
Aspartate transaminase	Myocardial infarction, liver diseases
Cholinesterase	Organophosphorus insecticide poisoning, hepatic parenchymal diseases
Creatine kinase	Myocardial infarction, muscle diseases
$\gamma$ -Glutamyl transferase	Hepatobiliary disease, alcoholism
Lactate dehydrogenase	Myocardial infarction, leukemia, muscular dystrophy, hepatic diseases
5'-Nucleotidase	Hepatitis, obstructive jaundice
Prostate specific antigen	Prostate cancer
Trypsin	Pancreatic disease, cystic fibrosis

# Plasma non-functional enzymes



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- ▶ 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 – examples of the latter are the cholinesterase variants.

# ASSESSMENT OF CELL DAMAGE AND PROLIFERATION

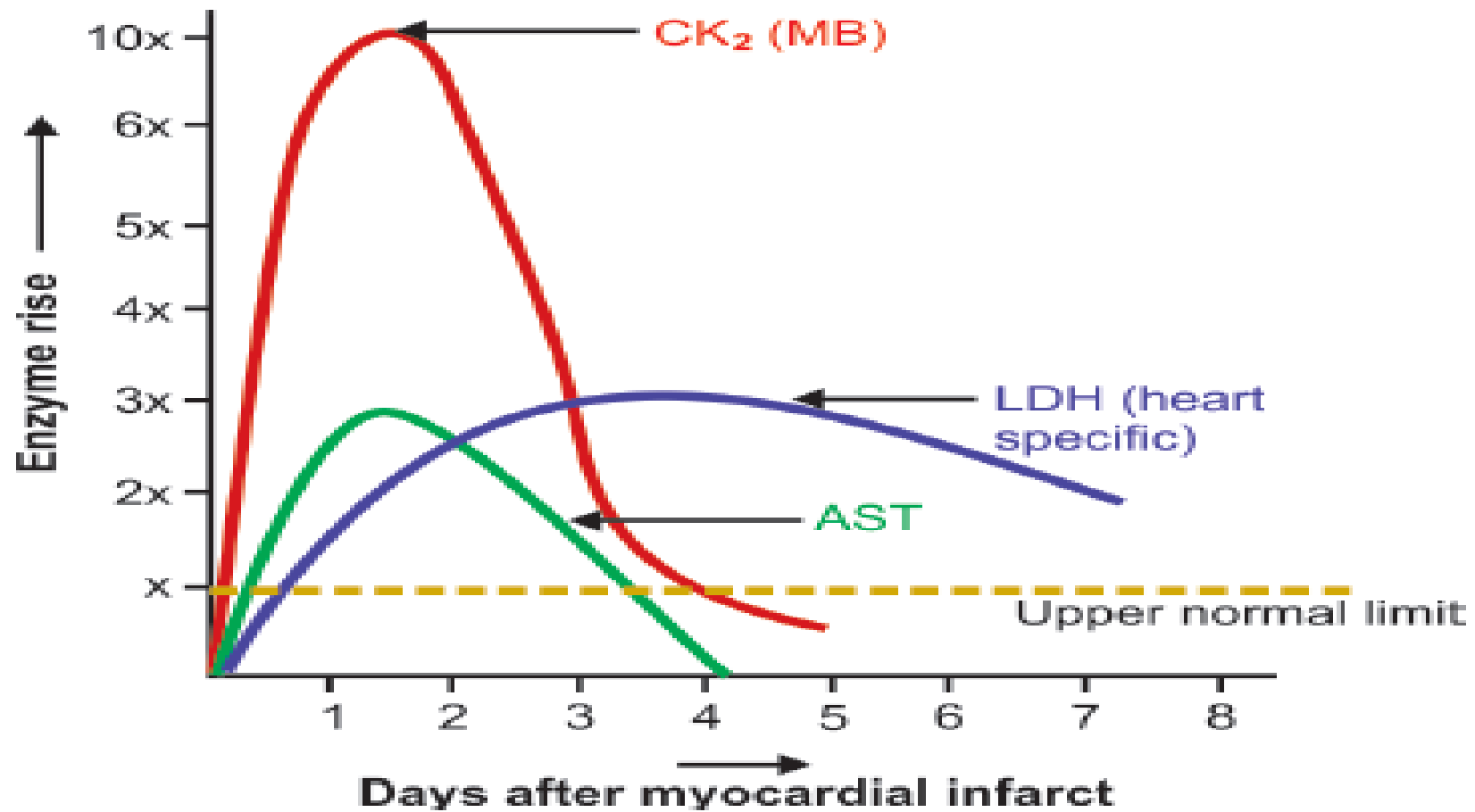
- ▶ **Not directly proportional**
- ▶ Acute: very high
- ▶ Chronic: moderately high/normal
- ▶ Very severe; low

# clearance

- ▶ Relatively small enzymes, such as amylase, can be cleared by the kidneys.
- ▶ Thus, plasma amylase activity may be high as a result of renal glomerular impairment rather than pancreatic damage.
- ▶ Larger enzymes cleared by reticuloendothelial system



# Biological half life



# Localization of damage

- ▶ May be specific for particular organ
- ▶ The distribution of enzymes within cells may differ.
- ▶ ALT and LDH are predominantly located in cytoplasm,
- ▶ Glutamate dehydrogenase in mitochondria
- ▶ AST occurs in both these cellular compartments.

# FACTORS AFFECTING RESULTS OF PLASMA ENZYME ASSAYS

- ▶ **Analytical factors**

- ▶ **Non-disease factors:**

age, gender, race, physiological conditions

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

- ▶ *Serial enzyme estimations*
- ▶ *Isoenzyme determination*
- ▶ *Estimation of more than one enzyme*

# Isoenzymes

Table 6.7: Examples of isoenzymes

<i>Enzyme</i>	<i>Isoenzyme forms</i>
Acid phosphatase	Prostate, erythrocytes, platelets, liver, spleen, kidney and bone marrow
Alkaline phosphatase	Bone, liver, placenta, intestine and kidney
Amylase	Salivary and pancreatic
Hexokinase	Liver (glucokinase) and muscle

Table 6.8: Type, composition, location and diagnostic importance of lactate dehydrogenase (LDH) and creatine kinase (CK) isoenzymes

<i>Type</i>	<i>Composition</i>	<i>Location</i>	<i>Diagnostic importance (cause of elevated level)</i>
LDH <sub>1</sub>	HHHH	Heart, RBC	Myocardial infarction
LDH <sub>2</sub>	HHHM	Heart, RBC	Megaloblastic anemia
LDH <sub>3</sub>	HHMM	Brain	Leukemia, malignancy
LDH <sub>4</sub>	HMMM	Lung, spleen	Pulmonary infarction
LDH <sub>5</sub>	MMMM	Liver, muscle	Liver diseases, Muscle damage/diseases
CK <sub>1</sub>	BB	Brain	Neurological injury
CK <sub>2</sub>	BM	Heart	Myocardial infarction
CK <sub>3</sub>	MM	Skeletal muscle	Muscular dystrophies and myopathies



# Therapeutic Use of Enzymes

Enzyme	Therapeutic use
<b>Bacterial asparaginase</b>	some types of leukemia
<b>Chymotrypsin</b>	dissolving ligaments of the lens during the extraction of cataract.
<b>Collagenase</b>	Used for debridement (cleaning of wound by removing dead tissue) of dermal ulcers and severe burns
<b>Pepsin, trypsin peptidase, lipase, amylase elastase</b>	gastrointestinal tract (GIT) disorders and chronic pancreatitis.
<b>Hyaluronidase</b>	promote the rapid absorption of drugs injected subcutaneously. It acts by increasing tissue permeability. It is used in the treatment of traumatic or postoperative edema
<b>Lysozyme</b>	used in the infection of eye
<b>Streptokinase</b>	myocardial infarction to dissolve blood clots



# Analytical Use of Enzymes

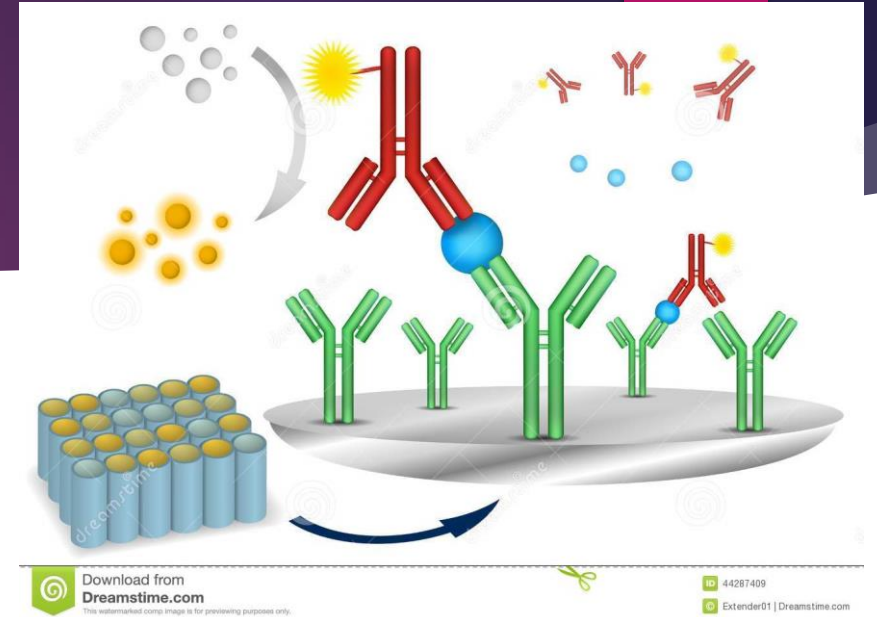
## ▶ As reagents

Enzyme	Used for testing
Urease	Urea
Uricase	Uric acid
Glucose oxidase	Glucose
Cholesterol oxidase	Cholesterol
Lipase	Triglyceride

# Analytical Use of Enzymes

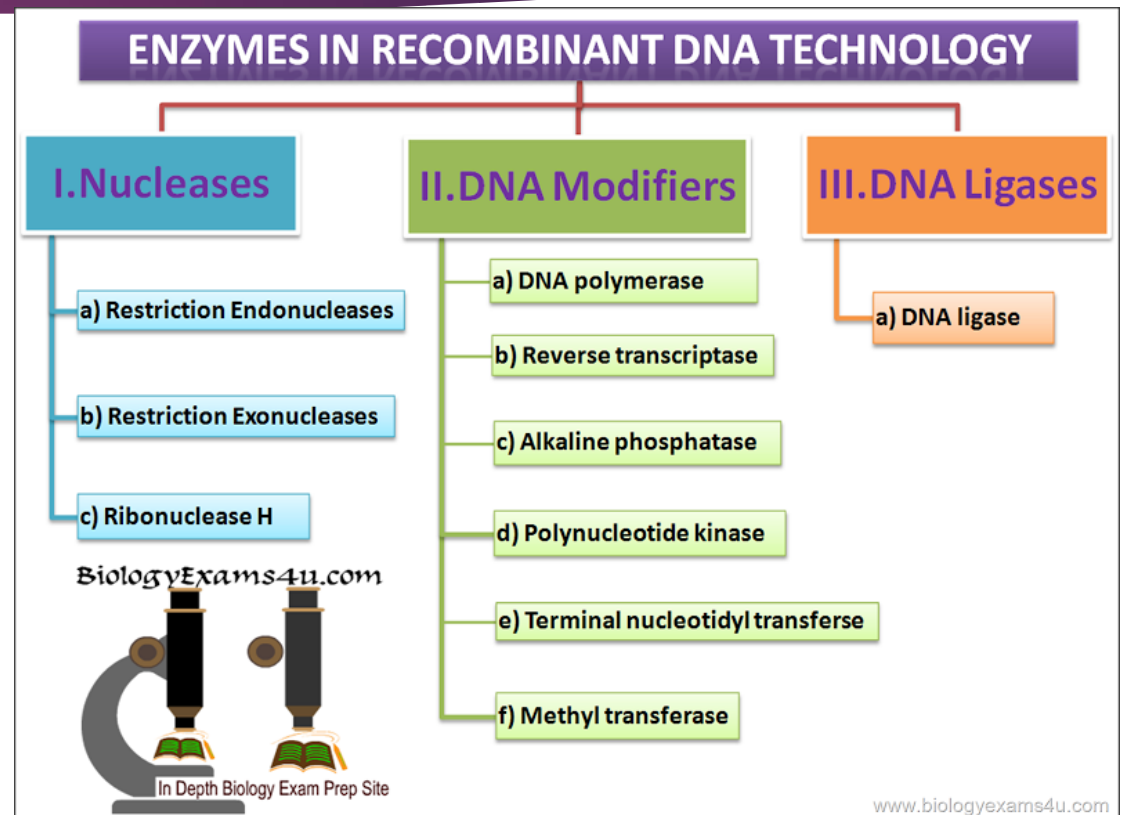
## ► As labels in ELISA

- Glucose-6-phosphate dehydrogenase
- Alkaline phosphatase
- $\beta$ -galactosidase
- Peroxidase



# Molecular Techniques

Restriction endonuclease  
Taq polymerase



Drugs	Product	Target Enzyme	Therapeutic Use
Allopurinol	Alloxanthin	Xanthine Oxidase	Gout
5-fluorouracil	Fluorodeoxy uridylate	Thymidylate synthase	Cancer
Aspirin	acetylates serine residue in the active center of cyclo-oxygenase	Cyclo-Oxygenase	Non Steroidal Anti-inflammatory Drug (NSAID)