Clinical Importance of Enzymes

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- Disorders
- Diagnosis of Diseases
- Pharmacologic agents and Gene Therapy

Enzymatic Diseases

- Thousand of diseases occurs due to enzymatic defects
- Most of them are rare and inherited
    - May affect Metabolic pathways: carbohydrate, lipid, proteins
    - May affect Physiological processes like digestion
    - May affect circulating enzyymes like antiproteases

Phenyl ketonuria

Phenylalanine

Phenylalanine Hydroxylase

Tyrosine

1 in 10000 live births

Mental Retardation

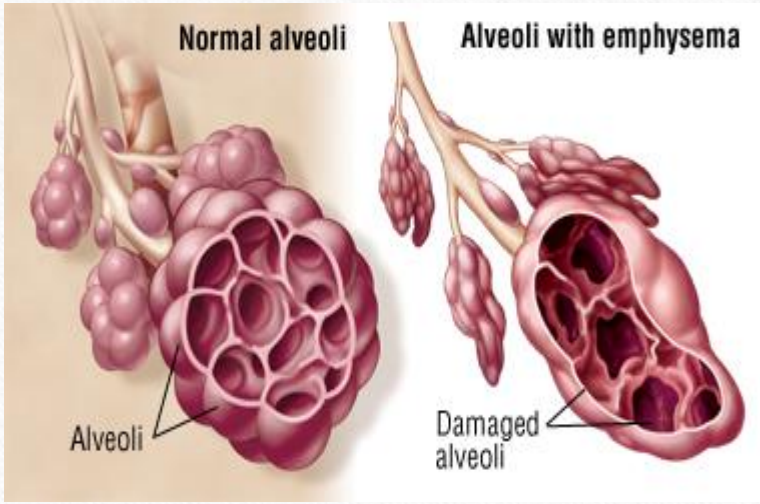
Albinism

Lactase Deficiency

- A very common disorder
- Milk indigestion
- Characterized by bloating, abdominal cramps and diarrhoea

Emphysema

- Due to **α 1 antitrypsin deficiency**
- Inhibitor of serine protease- Elastase
- Neutrophilic elastase inhibits bacterial growth
- Elastase may damage lung tissue elastin if escapes
- Kept in check by antiprotease α 1 antitrypsin



Diagnostic utility

Detection of Enzymes for diagnosis or prognosis of disease

Enzymes as analytical agent

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
Bone Enzymes	ALP , ACP

Plasma Functional Enzyme vs Plasma Nonfunctional enzymes

Plasma functional Enzyme

- Present in blood at all times
- Perform physiological functions in blood
- Eg. Lipoprotein lipase, Pseudocholinesterase, Clotting factors
- Decrease in diseased conditions like Liver disease

Plasma non-functional Enzymes

- Present in blood in minimal amounts
- No known physiological function in blood
- Eg. SGOT, SGPT, Amylase, CK-MB
- Increased in diseased conditions due to tissue damage, altered enzyme production

Isoenzymes

- Multiple forms of enzymes that catalyze the same reaction but differ in their structure
- Encoded by different structural gene loci
- Differ in physical properties like electrophoretic motility or resistance to heat inactivation
- Antigenically distinct
- Differ in catalytic properties like Km, Vmax.
- Shows Tissue specific distribution.

Examples of Isoenzymes

Enzyme	Isoenzymes
CK	CK-1 (CK-MM), CK-2 (CK-MB), CK-3 (CK-BB)
LDH	LDH 1-5
ALP	Hepatobiliary, Bone, Intestinal, Placental
Hexokinase	Hexokinase I-IV

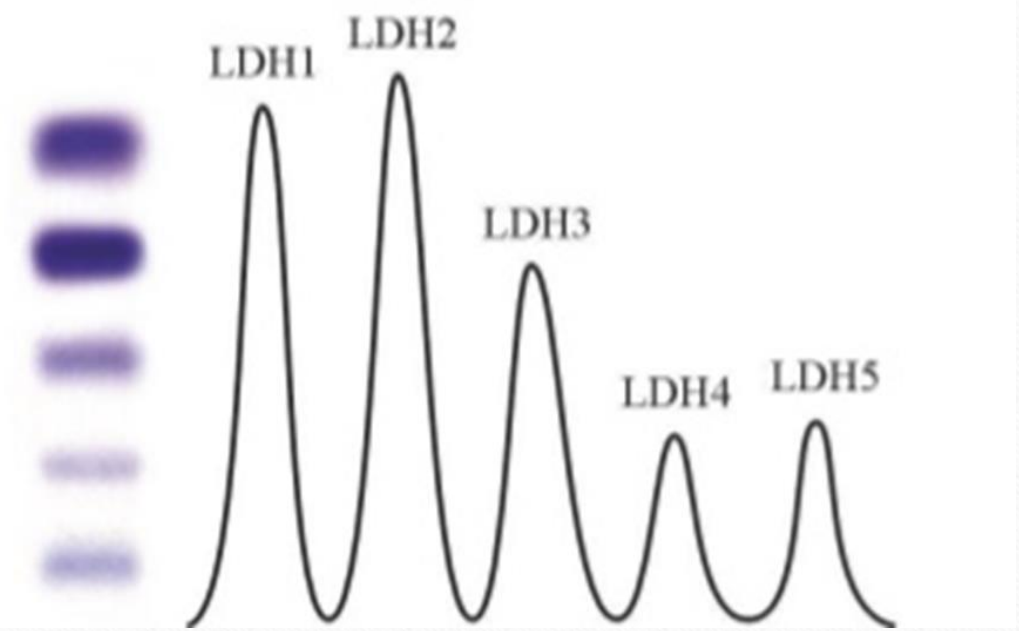
Methods for Iso-enzyme detection

- Electrophoresis
- ELISA/Ag-Ab reactions
- Sequencing
- Susceptibility to Inhibitors/ Inactivation

Lactate déshydrogénase LDH : 5 isoenzymes

2 gènes ⟶ 2 polypeptides : M(uscle) et H(eart)

association non covalente de 4 chaînes polypeptidiques H ou M



Clinical Scenario 1
Jaundice

- A 69 years old male presented with abdominal pain. His LFTs showed following results. His sclera was yellow and stools were pale with dark colored urine.

Tests	Result	Reference Range
Bilirubin	6.0mg/dl	0.3-1.2mg/dl
AST	34 U/L	<50 U/L
ALT	35 U/L	<50 U/L
ALP	870 U/L	30 – 120 U/L

Clinical Scenario 2
Jaundice

- A 35 years old male presented with malaise, weight loss, generalized weakness. He noticed dark colored urine for past 2 days. LFTs were as follows

Tests	Results	Reference Range
Bilirubin	2.5 mg/dL	0.3-1.2mg/dl
AST	900 U/L	<50 U/L
ALT	1200 U/L	<50 U/L
ALP	370 U/L	30 – 120 U/L

Clinical scenario 3
MI

- A 50 year male presented to ED with tight chest pain radiating to left arm. Cardiac function tests were as follows

Tests	Results	Reference Range
CK-Total	235 U/L	< 145 U/L
CK-MB	50 U/L	< 24 U/L
Troponin T	15 ng/L	< 10 ng/L

Enzymes as analytical reagents

- **Measurement of Metabolites**: Uricase, Urease, Glucose oxidase
- **Immunoassays**: ALP, Horse radish peroxidase, glucose 6 phosphate dehydrogenase
- **Recombinant DNA Technology:** Restriction Endonuclease, DNA ligase, DNA polymerase

Therapeutics

- Various drugs are used to inhibit enzymes therapeutically

Disorder	Enzyme	Drug
Cancer	Thymidylate Synthetase	5 fluorouracil
Inflammation	Cyclooxygenase	Aspirin
Gout	Xanthine oxidase	Allopurinol

Therapeutics

- Enzymes are also used as drugs

Disorder	Enzyme as Drug
MI	Streptokinase, tPA (Thrombolysis)
Gaucher's disease	Glucocerebrosidase (ERT/Gene Therapy)
Cystic Fibrosis	Trypsin

Summary

Disorders: Metabolic Pathways, Digestion, Circulating Enzymes

Diagnosis of Diseases: Biomarkers, Analytical agents, Recombinant DNA technology

Pharmacologic agents and **Gene Therapy**