

# 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 enzymes like antiproteases

## Phenyl ketonuria

Phenylalanine



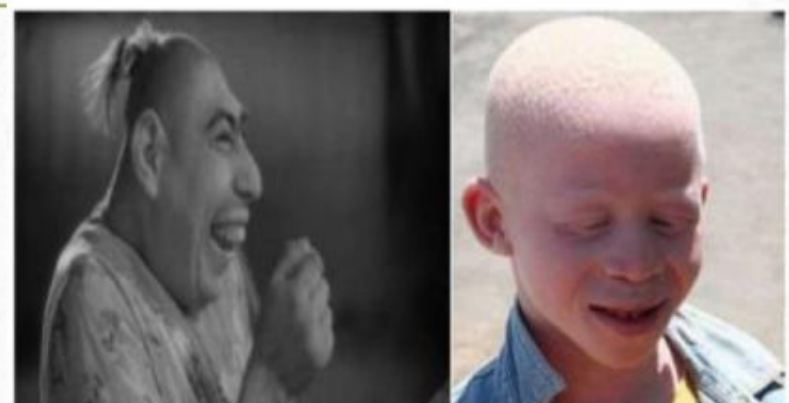
Phenylalanine Hydroxylase

Tyrosine

1 in 10000 live births

Mental Retardation

Albinism





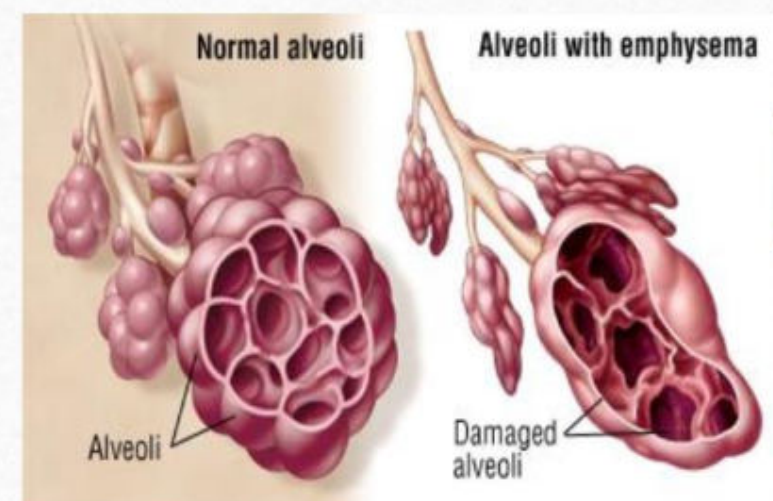
# Lactase Deficiency

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



# Emphysema

- Due to  $\alpha 1$  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  $\alpha 1$  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  $K_m$ ,  $V_{max}$ .
- Shows Tissue specific distribution.



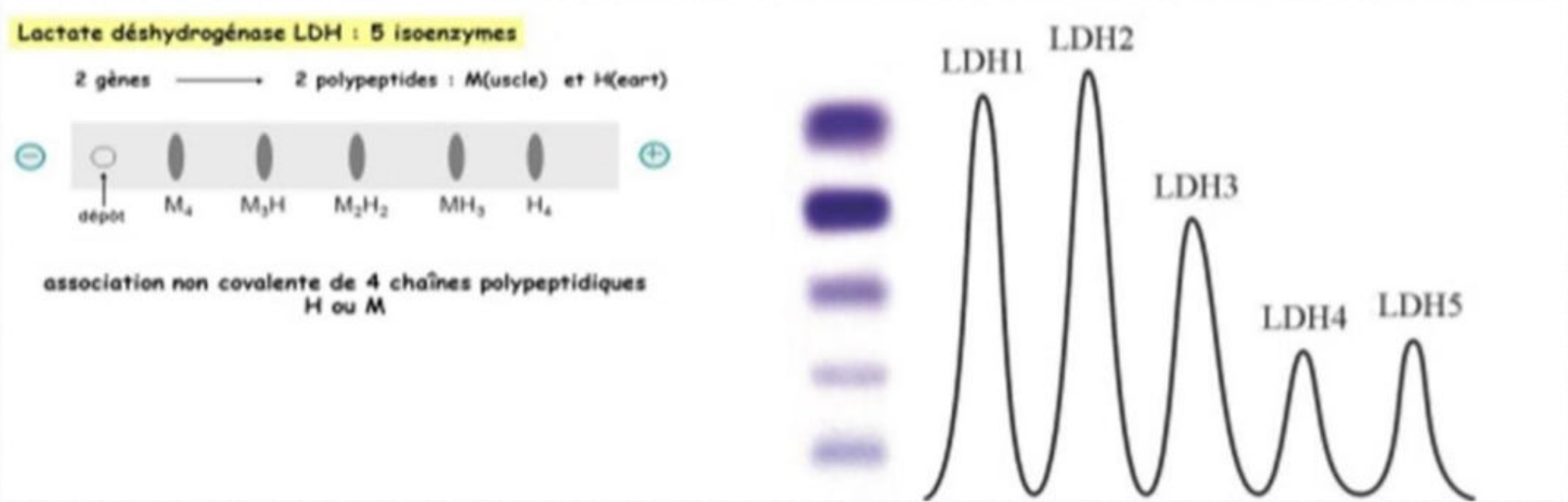
# Examples of Isoenzymes

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





# 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