

Enzymes in Clinical Biochemistry

You are supposed to know ...

- Enzymes – main features, properties
- Coenzymes – structures, functions
- Enzyme kinetics
- Enzyme activity

Isoenzymes – General Features

- Genetically determined differences in primary structure
- Catalyze the same reaction
- May have **different subcellular distribution**
(cytoplasm × mitochondria)
- May have **different tissue distribution**
- May be combined from more subunits (quarternary structure)
- May differ in kinetic properties (K_M)
- Usually are determined by electrophoresis

Q. 2 (p. 27)

Explain the terms: proenzyme, isoenzyme, isoform

A. 2

- **Proenzyme** (zymogen) – inactive form of enzyme that becomes active after partial proteolysis
example: pepsinogen → pepsin
- **Isoenzyme** – see previous page
- **Isoform** – more general term, includes true isoenzymes and pseudoisoenzymes (posttranslational variations)

Lactate dehydrogenase (LD)

- **Tetramer**
- Two different chains (H - heart, M - muscle)
- Five isoenzymes:
LD₁ (H₄), **LD₂** (H₃M), **LD₃** (H₂M₂), **LD₄** (HM₃), **LD₅** (M₄)
- Widely distributed in body
- Total activity determination – nonspecific finding
- LD₁ + LD₂ marker of myocardial infarction (MI)
- Today is LD assay considered out-of-date




Creatine kinase (CK)

- **Dimer**
- Two different chains (M – muscle, B – brain)
- Three isoenzymes: **MM** (muscle), **MB** (heart), **BB** (brain)
- Major isoenzyme in blood is MM (95 %)
- MB form in blood: 0 – 6 %
- BB in blood: traces (BB cannot pass across blood-brain barrier)
- MB isoenzyme excellent marker of myocardial infarction

Enzymes in Blood

Feature	Plasmatic enzymes	Secretory enzymes	Intracellular enzymes
Example	coag. factors	amylase, lipase	AST, ...
Source organ	liver	pancreas	various
Function in	blood	GIT	cells
Enzyme activity in blood after source organ damage	?	?	?

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Q. 6

Why are low activities of cellular enzymes detected even in serum of healthy people?

A. 6

Low activities of intracellular enzymes
in extracellular fluid (blood plasma, serum)
are the consequence
of physiological cell disintegration.

Main Tissue Distribution of Enzymes

AST	liver, myocard
ALT	liver
LD	not specific
CK	myocard, muscles
GMT	liver
ALP	biliary tract, bones
ACP	prostate
AMS	pancreas
LPS	pancreas
CHS	liver

Intracellular Location of Enzymes

Intracellular Location	Enzymes
Cytoplasm	LD, ALT, 30 % AST
Mitochondria	70 % AST
Golgi complex, ER	CHS, AMS
Lysosome	ACP
Membrane	GMT, ALP

Consider the AST/ALT ratio

- $AST/ALT > 1$ severe liver damage
- $AST/ALT < 1$ mild liver damage

Enzymes of Clinical Significance

Enzyme	Source of blood elevation
ALT	hepatopathy
AST	MI, hepatopathy
GMT	hepatopathy (alcohol, drugs)
ALP	biliary tract diseases, bone diseases
ACP	prostatic cancer
CK	MI (CK-MB), muscle diseases
AMS	pancreatitis
LPS	pancreatitis
CHS	hepatopathy (alcohol, drugs) – decreased

Catalytic concentration of some enzymes

Enzyme	Reference values (serum)
ALT	0.1 - 0.9 $\mu\text{kat/l}$
AST	0.1 - 0.7 $\mu\text{kat/l}$
LD	up to 7.5 $\mu\text{kat/l}$
CK	up to 4 $\mu\text{kat/l}$

see also the lab manual

Q. 7

What enzymes might appear in blood

- a) In mild hepatocellular damage
- b) In serious hepatocellular damage

A. 7

a) Mild hepatocellular damage:

enzymes from cytoplasm and/or membrane are released into ECF – ALT, GMT, ALP

b) Severe hepatocellular damage:

enzymes from mitochondria are released into ECF – AST

Q. 8

Write equations of reactions catalyzed by:

ALT

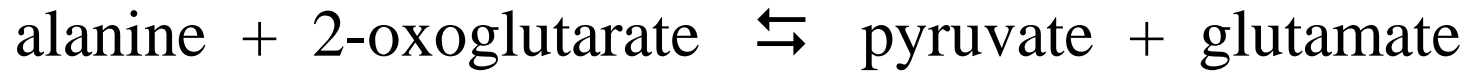
AST

LD

ALT Reaction



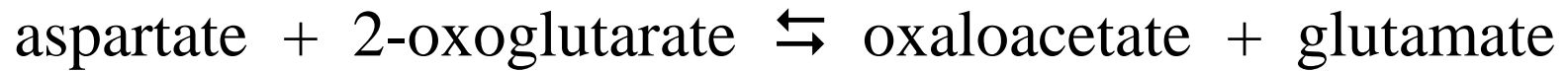
ALT Reaction



AST reaction

aspartate + 2-oxoglutarate \rightleftharpoons

AST reaction



LD reaction



LD reaction



Q. 9

The levels of most blood enzymes are increased in newborns and infants. What enzyme persists elevated till puberty?

A. 9

ALP – the bone isoenzyme activity persists till puberty

Biochemical Diagnostic of MI

Enzyme / Protein	Half-time (hrs)
Myoglobin	0,25
Troponine T cardiac form	2
CK-MB	13
AST	17
LD ₁₂	110

