

Clinical Enzymology and Biomarkers

? CLINICAL ENZYMOLOGY & BIOMARKERS

(CK, Troponins, LDH, Cardiac Disease Markers)

Structured in your MedMentor format—crisp, conceptual, and ready for students.

? CREATINE KINASE (CK / CPK)

? Basics

- Enzyme of **muscle energy metabolism**.
- Converts:
Creatine + ATP ? Creatine phosphate + ADP

? Isoenzymes (Very Important)

ISOENZYME	LOCATION	CLINICAL USE
CK-BB (CK1)	Brain, lung	CNS injury
CK-MB (CK2)	Heart	MI marker
CK-MM (CK3)	Skeletal muscle	Muscle injury, rhabdomyolysis

? CK-MB in Myocardial Infarction

- **Rises:** 3–6 hours

- **Peak:** 18–24 hours
- **Returns to normal:** 2–3 days
- Useful for **detecting reinfarction** because it falls early.

? Conditions with ? CK

- MI (CK-MB)
- Myocarditis
- Duchenne muscular dystrophy
- Rhabdomyolysis
- Polymyositis
- Hypothyroidism
- Seizures, trauma

? CARDIAC TROPONINS (cTnI, cTnT)

(Most sensitive & specific markers of myocardial injury)

? Components

- **Troponin C:** Calcium binding
- **Troponin I:** Inhibitory subunit
- **Troponin T:** Tropomyosin-binding

- Cardiac forms are **unique**, so highly specific.

? Troponin Timeline

- **Rises:** 3–4 hours
- **Peak:** 24–48 hours
- **Stay elevated:** 7–14 days (very long)

? Advantages

- Most specific marker for MI
- Detected early
- Useful even in small non-STEMI
- Remains elevated long after CK-MB normalizes

? Conditions causing high troponin

- MI
- Myocarditis
- Takotsubo cardiomyopathy
- Sepsis
- Renal failure
- Severe pulmonary embolism

- Heart failure (acute)

? LACTATE DEHYDROGENASE (LDH)

? Reaction

Converts:

Lactate ? Pyruvate

? Isoenzymes

ISOENZYME	ORGAN	NOTE
LDH1	Heart, RBCs	Flipped pattern in MI
LDH2	Heart, RBCs	Normally > LDH1
LDH3	Lung	Pneumonia, pulmonary infarct
LDH4	Kidney, pancreas	Renal diseases
LDH5	Liver, muscle	Liver injury, rhabdomyolysis

? LDH in MI

- **LDH1 > LDH2 (flipped pattern)** = classic sign of MI
- **Rises:** 12–24 hours
- **Peaks:** 2–3 days
- **Duration:** 7–10 days

- Useful when patient presents late.

? Conditions where LDH is elevated

- MI
- Hemolysis
- Megaloblastic anemia
- Liver disease
- Cancer
- Muscle injury
- Kidney disease

? BIOMARKERS OF CARDIAC DISEASES (FULL PANEL)

? 1. Most Important:

- **Troponin I & T** ? gold standard
 - **CK-MB** ? reinfarction detection
 - **Myoglobin** ? earliest marker but nonspecific
-

? 2. Timeline Comparison

MARKER	RISE	PEAK	NORMALIZATION
Myoglobin	1–2 h	6–9 h	24 h
CK-MB	3–6 h	18–24 h	2–3 d
Troponin I/T	3–4 h	24–48 h	7–14 d
LDH	12–24 h	2–3 d	7–10 d

? 3. Other Cardiac Markers

? BNP & NT-proBNP

- From ventricles during stretch ? marker of **heart failure**.

? HS-CRP

- Marker of inflammation
- Predictor of **atherosclerosis** and CV risk.

? AST (SGOT)

- Mildly elevated in MI but nonspecific.

? Copeptin

- Released early after MI; used with troponin as dual marker.

? Key High-Yield Concepts

- **Troponin** = best, most specific MI marker.
- **CK-MB** = best for reinfarction detection.
- **LDH1/LDH2 flip** = late MI marker.
- **Myoglobin** = earliest rising but poorest specificity.
- **BNP** = heart failure marker.
- **High troponins may occur without MI** in renal failure and sepsis.

? ASPARTATE AMINOTRANSFERASE (AST / SGOT)

? Basic Function

- Catalyzes:
Aspartate + α -ketoglutarate $\rightarrow$ Oxaloacetate + Glutamate
- Requires **pyridoxal phosphate (Vitamin B6)**.

? Location

- Highly concentrated in:
 - **Heart**
 - **Liver**

- **Skeletal muscle**
- Kidneys
- RBCs

? Clinical Uses

- Marker of **hepatocellular injury**
- Also elevated in **muscle injury**, **cardiac injury**, hemolysis

? AST/ALT Ratio

- **AST : ALT > 2 ? Alcoholic liver disease** (very high-yield)
- **AST > ALT ?** Cirrhosis, muscle disease
- **ALT > AST ?** Viral hepatitis (usually)

? Conditions where AST increases

- Acute viral hepatitis
 - Alcoholic hepatitis
 - Myocardial infarction
 - Muscle trauma, rhabdomyolysis
 - Hemolysis
-

? ALANINE AMINOTRANSFERASE (ALT / SGPT)

? Basic Function

- Catalyzes:
Alanine + ?-ketoglutarate ? Pyruvate + Glutamate
- Requires **Vitamin B6**.

? Location

- **Most specific enzyme for liver injury**
- Highest concentration in **hepatocytes**.

? Clinical Significance

- Best marker for **hepatocellular damage**.
- ALT rises higher and stays elevated longer than AST in **acute viral hepatitis**.

? ALT Dominance

- **ALT > AST** in:
 - Viral hepatitis
 - Toxic hepatitis
 - Non-alcoholic fatty liver disease (NAFLD)
 - Drug-induced liver injury (DILI)

? Massive ALT elevations

Seen in:

- Acute viral hepatitis
- Acetaminophen toxicity
- Ischemic hepatitis

? ALKALINE PHOSPHATASE (ALP)

? Function

- Hydrolyzes phosphate esters at **alkaline pH (optimal pH ~9–10)**.

? Major Sources

- **Liver (bile canaliculi)**
- **Bone (osteoblasts)**
- Intestine
- Placenta
- Kidney

? Liver ALP

- Elevated in **cholestasis** (bile obstruction).
- Increased in:

- Extrahepatic obstruction (stones, tumors)
- Intrahepatic cholestasis
- Primary biliary cholangitis
- Primary sclerosing cholangitis

? Bone ALP

- Elevated when bone turnover is high:
 - Rickets
 - Osteomalacia
 - Paget disease
 - Bone metastasis
 - Hyperparathyroidism
 - Healing fractures

? Differentiation of ALP Source

- GGT (Gamma-glutamyl transferase):
 - ? ALP + ? GGT ? **Hepatobiliary origin**
 - ? ALP + normal GGT ? **Bone origin**

? Physiological Rise in ALP

- Pregnancy (placental ALP)
- Adolescence (bone growth)
- Third trimester

? ULTRA-SHORT SUMMARY

- **AST** ? Heart + Liver + Muscle (Alcohol > Viral)
- **ALT** ? Most specific for liver (Viral > Alcohol)
- **ALP** ? Cholestasis & Bone turnover marker
- **AST:ALT > 2** ? Alcoholic hepatitis
- **ALP ? + GGT ? ?** Obstructive liver disease
- **ALP ? + GGT normal** ? Bone disorder

? NUCLEOTIDE PHOSPHATASE (NTP / 5'-Nucleotidase)

? Basic Function

- Hydrolyzes **5'-nucleotides** ? nucleosides + phosphate.
- Works at **alkaline pH**, similar to ALP.

? Where is it found?

- **Liver (bile canalicular membranes)**

- Also present in:

- Kidney
- Intestine
- Pancreas
- Brain

? Clinical Importance

- **Very sensitive marker of cholestasis.**
- Especially useful when ALP is elevated but the source is unclear (bone vs liver).

? Differentiation

MARKER	HIGH IN LIVER DISEASE?	HIGH IN BONE DISEASE?
ALP	Yes	Yes
GGT	Yes	No
5'-Nucleotidase	Yes	No

? Therefore:

? ALP + ? 5'-Nucleotidase = Liver source

? ALP + normal 5'-Nucleotidase = Bone source

? Conditions with Elevated 5'-Nucleotidase

- Cholestasis (intra & extrahepatic)
- Primary biliary cholangitis
- Primary sclerosing cholangitis
- Drug-induced cholestasis
- Metastatic liver disease

? GAMMA-GLUTAMYL TRANSFERASE (GGT)

? Basic Function

- Transfers **γ-glutamyl groups** in glutathione metabolism.
- Helps amino acid transport.

? Major Sources

- **Liver (highest)**
- Kidney
- Pancreas
- Intestine
- Prostate

? Clinical Importance

- **Highly sensitive marker of cholestasis & hepatobiliary disease.**
- Often elevated earlier than ALP.

? Differentiation

- **GGT ? + ALP ? ? hepatobiliary cause.**
- **GGT normal + ALP ? ? bone disease.**

? GGT is strongly induced by:

- **Alcohol intake**
- **Drugs** such as phenytoin, phenobarbital ? microsomal enzyme induction

? Conditions with ? GGT

- Alcoholic liver disease
- Fatty liver
- Biliary obstruction
- Chronic cholangitis
- Pancreatic disease
- Hepatotoxic drugs

? MARKERS OF LIVER DISEASES (Complete High-Yield Set)

Organize liver biomarkers by **type of liver injury**:

? 1. Hepatocellular Injury Markers

? ALT (SGPT)

- Most specific marker of **liver cell injury**.
- Higher than AST in **viral, toxic, ischemic hepatitis**.

? AST (SGOT)

- Elevated in liver, muscle, and heart injury.
- **AST:ALT > 2** ? alcoholic hepatitis.

? LDH (Liver Isoenzyme LDH5)

- Mild elevation in hepatitis.
- High LDH with normal ALT suggests **ischemic hepatitis**.

? 2. Markers of Cholestasis / Biliary Obstruction

? Alkaline Phosphatase (ALP)

- From bile canalicular cells.
- Markedly elevated in **obstructive jaundice**.

? GGT

- Elevated in liver obstruction & alcohol intake.

- Helps differentiate liver ALP from bone ALP.

? 5?-Nucleotidase

- Highly specific for **cholestasis**.
- Not increased in bone diseases.

? 3. Markers of Synthetic Function of Liver

? Albumin

- Decreased in chronic liver disease.

? Prothrombin time (PT/INR)

- Prolonged in **acute liver failure** (short half-life factor VII).

? Cholesterol

- Often decreased in advanced liver disease.

? 4. Markers of Hepatic Clearance

? Bilirubin

- **Unconjugated ?**: hemolysis, Gilbert, Crigler–Najjar
- **Conjugated ?**: cholestasis, Dubin–Johnson, Rotor, hepatocellular injury

? Ammonia

- Elevated in hepatic encephalopathy.

? 5. Markers of Alcoholic Liver Disease

- **GGT ??** (enzyme induction)
- **AST:ALT > 2:1**
- Macrocytosis (MCV ?)
- High triglycerides
- Low magnesium

? 6. Markers of Cirrhosis

- ? Albumin
- ? INR
- ? Bilirubin
- ? Platelets (splenic sequestration)
- ? GGT and ALP (if cholestatic component)

? 7. Markers of Liver Tumors

- **AFP (Alpha-fetoprotein)** ? hepatocellular carcinoma

- **ALP & GGT** ? ? metastatic liver disease

? Ultra-Short Summary (Rapid Revision)

- **ALT** = Most specific for liver injury
- **AST:ALT > 2** = Alcoholic hepatitis
- **ALP ? + GGT ?** = Cholestasis
- **ALP ? + GGT normal** = Bone disease
- **5?-Nucleotidase** = Specific for cholestasis
- **GGT** = Alcohol, drugs, liver
- **Albumin & INR** = Liver synthetic function
- **PT prolongation** = Acute liver failure
- **AFP** = HCC marker

? ACID PHOSPHATASE (ACP)

? Basic Function

- Hydrolyzes phosphate esters **at acidic pH (~5)**.
- Present in lysosomes.

? Sources

- Prostate (highest concentration)
 - RBCs
 - Platelets
 - Liver
 - Spleen
 - Bone (osteoclasts)
-

? Clinical Importance

? 1. Prostatic ACP

- Marker of **prostate carcinoma** (especially metastatic).
- Historically used ? now replaced by **PSA**, but still asked in exams.

? 2. Tartrate-resistant acid phosphatase (TRAP)

- Increased in:
 - **Hairy cell leukemia (very high-yield)**
 - Osteoclast activity (Paget disease)

? 3. RBC ACP

- Elevated in **Gaucher disease** and **Niemann–Pick disease**.

? 4. Bone disorders

- Osteolytic lesions
- Paget disease
- Hyperparathyroidism

? CHOLINESTERASE

Two types:

? 1. True Cholinesterase (Acetylcholinesterase)

- Found in **RBCs, nerves, neuromuscular junctions**.
- Rapidly hydrolyzes acetylcholine.

? 2. Pseudocholinesterase (Butyrylcholinesterase / Plasma ChE)

- Synthesized in **liver**.
 - Found in **plasma, liver, pancreas**.
 - Important for **drug metabolism**.
-

? Clinical Importance

? Low Plasma Cholinesterase Levels

Indicates impaired hepatic synthesis or inhibition.

Seen in:

- **Liver failure**
- **Organophosphate poisoning** (irreversible inhibition)
- Malnutrition
- Pregnancy (normal physiological decrease)
- Genetic variants (atypical pseudocholinesterase)
- Certain drugs:
 - Succinylcholine
 - Echothiophate
 - Neostigmine

? Atypical Cholinesterase (Genetic)

- Patients show **prolonged apnea** after **succinylcholine** because they cannot break it down.
- Detected using **dibucaine number**.

? Dibucaine Number

- Normal: > **80% inhibition**
- Heterozygous atypical: **40–70%**
- Homozygous atypical: < **20%**

? GLUCOSE-6-PHOSPHATE DEHYDROGENASE (G6PD)

? Basic Function

- First enzyme of the **HMP (pentose phosphate) pathway**.
- Produces **NADPH**, which keeps **glutathione (GSH)** in reduced form.
- GSH protects RBCs from oxidative damage.

? Why RBCs Need G6PD?

- RBCs lack mitochondria ? **NADPH only from HMP shunt**.
- Without NADPH ? oxidative stress ? hemolysis.

? G6PD Deficiency

- X-linked recessive disorder.
- Most common enzyme defect in humans.

- RBCs are vulnerable to oxidative stress.
-

? Triggers for Hemolysis

- **Drugs:**
 - Antimalarials (primaquine)
 - Sulfonamides
 - Nitrofurantoin
 - Dapsone
 - **Infections**
 - **Fava beans (favism)**
 - **Naphthalene (mothballs)**
-

? Mechanism

Oxidative stress ? RBC membrane damage ? Hb precipitates into **Heinz bodies** ? removed by spleen ? **bite cells** ? hemolytic anemia.

? Laboratory Features

- ? Reticulocyte count

- ? Indirect bilirubin
 - ? Haptoglobin
 - **Heinz bodies** (crystal violet stain)
 - **Bite cells** on peripheral smear
-

? Diagnostic Test

- **G6PD assay** (after hemolysis resolves to avoid false normal result)
 - **Fluorescent spot test**
-

? Clinical Presentations

- Acute hemolytic crisis after drug/fava beans
 - Neonatal jaundice
 - Chronic nonspherocytic hemolytic anemia (rare variant)
-

? Ultra-Short Summary (Final Revision)

- **ACP:** prostate cancer marker; TRAP ? in hairy cell leukemia.
- **Cholinesterase:** ? in liver failure & organophosphate poisoning; dibucaine number confirms atypical variant.

- **G6PD**: NADPH producer; deficiency ? Heinz bodies + bite cells after oxidative stress.

? AMYLASE

? Function

- Hydrolyzes **starch ? maltose & dextrins**.
- Works at **neutral pH**.

? Types

1. **Pancreatic amylase (P-type)**
2. **Salivary amylase (S-type)**

? Sources

- Pancreas
- Salivary glands
- Fallopian tubes
- Small intestine

? Clinical Significance

? Hyperamylasemia occurs in:

- **Acute pancreatitis (most important)**
- Pancreatic trauma
- Gallstone obstruction
- Mumps (salivary gland inflammation)
- Renal failure (reduced clearance)
- Macroamylasemia (bound to Ig; benign)

? Values in Acute Pancreatitis

- Rises: **3–6 hours**
- Peaks: **24–30 hours**
- Returns to normal: **2–4 days**

? Urine Amylase

- Stays elevated longer than serum.
- Useful when serum values normalize early.

? LIPASE

? Function

- Hydrolyzes **triglycerides ? fatty acids + glycerol**.

- Produced in **pancreatic acinar cells**.

? Clinical Importance

- **Most specific marker for acute pancreatitis** (more specific than amylase).

? Timeline in Acute Pancreatitis

- Rises: **4–8 hours**
- Peaks: **24 hours**
- Remains elevated: **8–14 days**

? Advantages over Amylase

- More specific to pancreas.
- Remains elevated longer.
- Not affected by salivary gland disease.

? Elevated Lipase also seen in:

- Pancreatic cancer
- Perforated peptic ulcer
- Intestinal obstruction
- Renal failure
- Cholecystitis

? ALDOLASE

? Function

- Enzyme of glycolysis:
Fructose-1,6-bisphosphate → DHAP + G3P

? Sources

- **Skeletal muscle**
- **Heart muscle**
- Liver
- Brain

? Clinical Importance

Historically used for **muscle diseases**, but now partly replaced by CK.

? High Aldolase in:

- **Duchenne muscular dystrophy**
- Inflammatory myopathies:
 - Polymyositis
 - Dermatomyositis
- Hepatitis
- Myocardial infarction

? Aldolase vs CK

- Aldolase rises in **muscle disease when CK is normal** (e.g., some myopathies).

? ENOLASE

? Function

- Glycolytic enzyme:
2-phosphoglycerate ? phosphoenolpyruvate (PEP)

? Isoenzymes

1. **Neuron-specific enolase (NSE)** ? brain
2. Muscle enolase
3. Non-specific enolase

? Clinical Importance

? Neuron-Specific Enolase (NSE)

Tumor marker for:

- **Small cell lung carcinoma (SCLC)**
- Neuroblastoma
- Pancreatic endocrine tumors

? Elevated NSE also seen in:

- Stroke
- Brain injury
- Subarachnoid hemorrhage

? NSE is the tumor marker of choice for SCLC.

? Ultra-High Yield Summary

- **Amylase** ? ? acute pancreatitis, mumps, renal failure.
- **Lipase** ? ? *most specific* for acute pancreatitis (stays elevated longer).
- **Aldolase** ? ? muscle diseases like DMD, polymyositis.
- **NSE** ? ? small cell lung carcinoma, neuroblastoma.

? ENZYMES AS THERAPEUTIC AGENTS

Enzymes used as **drugs** for treatment of various conditions.

? 1. Thrombolytic / Fibrinolytic Enzymes

Used to dissolve blood clots.

- **Streptokinase**
 - From *Streptococcus*.

- Activates plasminogen → plasmin.
- Used in MI, DVT, pulmonary embolism.

- **Urokinase**

- Direct plasminogen activator.
- Used in pulmonary embolism.

- **tPA (Tissue Plasminogen Activator) / Alteplase**

- Recombinant human enzyme → very specific.
 - Used in acute MI, ischemic stroke.
-

? 2. Digestive Enzymes

- **Pancreatin / Pancrelipase**

- Lipase, amylase, proteases.
- Used in chronic pancreatitis, CF.

- **Lactase**

- Used in lactose intolerance.
-

? 3. Anti-inflammatory Enzymes

- **Serratiopeptidase** (proteolytic enzyme)
 - Reduces swelling, inflammation.
 - **Chymotrypsin / Trypsin**
 - Used in wound debridement.
-

? 4. Enzyme Replacement Therapy (ERT)

Used in genetic enzyme deficiencies.

- **Imiglucerase** for Gaucher disease
 - **Laronidase** for Hurler syndrome
 - **Idursulfase** for Hunter syndrome
 - **Agalsidase** for Fabry disease
-

? 5. Anticancer / Chemotherapy-related Enzymes

- **Asparaginase (L-Asparaginase)**
 - Used in ALL (acute lymphoblastic leukemia).
 - Depletes asparagine ? kills leukemic cells.
-

? 6. Deoxyribonuclease (DNase)

- **Dornase alfa** (DNase I)
 - Used in cystic fibrosis to reduce sputum viscosity.

? 7. Hyaluronidase

- Depolymerizes hyaluronic acid.
- Used to increase drug absorption, reduce edema, and in ophthalmic surgery.

? ENZYMES USED FOR DIAGNOSIS

Enzymes measured in blood or tissues to diagnose diseases.

? 1. Cardiac Markers

- **CK-MB** ? myocardial infarction
 - **Troponins** (T, I) ? most specific for MI
 - **LDH1 > LDH2 flip** ? late MI
-

? 2. Hepatobiliary Markers

- **ALT, AST** ? hepatocellular injury
 - **ALP, GGT, 5?-nucleotidase** ? cholestasis
 - **LDH5** ? liver damage
-

? 3. Pancreatic Markers

- **Amylase, Lipase** ? acute pancreatitis
 - **Lipase** is more specific.
-

? 4. Bone Markers

- **Bone ALP** ? rickets, Paget disease, bone metastasis
 - **ACP (osteoclast)** ? bone turnover
-

? 5. Muscle Markers

- **CK-MM** ? skeletal muscle injury
 - **Aldolase** ? myopathies (DMD, polymyositis)
-

? 6. Prostatic Marker

- **Acid phosphatase (ACP)** ? historically used in prostate cancer
 - Now replaced by PSA, but still asked in exams.
-

? 7. Tumor Marker Enzymes

- **Neuron-specific enolase (NSE)** ? small cell lung carcinoma, neuroblastoma
 - **Placental ALP** ? seminoma
-

? 8. Metabolic Disorders

- **G6PD assay** ? G6PD deficiency
 - **Galactose-1-phosphate uridyl transferase** ? galactosemia
-

? IMMOBILIZED ENZYMES

Enzymes fixed onto a solid support so they can be **reused**, stabilized, or continuously used.

? Why Immobilize Enzymes?

- Reuse of expensive enzymes
 - Increased stability (temperature/pH)
-

- Easy separation from products
 - Continuous operation in bioreactors
 - Increased shelf-life
-

? Methods of Immobilization

? 1. Adsorption

- Physical binding on carriers (charcoal, resins).
- Simple, but enzyme may leach out.

? 2. Covalent Bonding

- Strong binding to support (agarose, silica).
- More stable but may reduce activity.

? 3. Entrapment

- Trapped in polymer matrix (alginate, polyacrylamide).
- Substrate must diffuse in and out.

? 4. Encapsulation

- Enzymes enclosed in semipermeable membranes.

? 5. Cross-linking

- Enzymes linked with bifunctional reagents (glutaraldehyde).
 - Forms large, stable aggregates (CLEAs).
-

? Applications of Immobilized Enzymes

? 1. Industrial

- Glucose isomerase ? **HFCS manufacture**
- Lactase ? lactose-free milk
- Lipases ? biodiesel production
- Proteases ? detergent industry

? 2. Clinical

- Urease electrodes ? biosensors
- Glucose oxidase ? **glucose biosensors (glucometers)**

? 3. Research

- Immobilized DNases and RNases
- Immobilized proteases for digestion in mass spectrometry

? Ultra-Short Summary

- **Streptokinase, alteplase** ? thrombolytics.
- **Asparaginase** ? ALL treatment.
- **Pancrelipase** ? chronic pancreatitis.
- **ALT/AST** ? liver injury; **ALP/GGT** ? cholestasis.
- **CK-MB, troponins** ? MI diagnosis.
- **NSE** ? small cell carcinoma.
- **Immobilized enzymes** ? glucose oxidase for glucometers; glucose isomerase for HFCS.

? IMPORTANT POINTS TO REMEMBER — Clinical Enzymology & Biomarkers

These are crisp, high-value facts that students reliably get asked in theory, MCQs, and viva.

? GENERAL PRINCIPLES

- Enzymes leak into blood when **cells are damaged**.
 - **Tissue specificity** of an enzyme determines its diagnostic value.
 - Isoenzymes help localize disease (e.g., CK-MB for heart, LDH isoenzymes for organs).
 - Half-life of enzymes determines usefulness in early or late diagnosis.
-

? CARDIAC ENZYMES

? Troponins (cTnI, cTnT)

- **Most specific & sensitive** markers of MI.
- Rise: **3–4 h**, Peak: **24–48 h**, Stay high: **7–14 days**.
- Useful for **late presentation**.

? CK-MB

- Rises early and falls early ? best to detect **reinfarction**.
- Rise: **3–6 h**, Normal: **48–72 h**.
- CK-MB > 5% of total CK strongly suggests MI.

? LDH Isoenzymes

- **LDH1 > LDH2** (flip) = classic sign of **late MI**.
- Remains elevated for **7–10 days**.

? Myoglobin

- **Earliest** marker (1–2 h) but not specific.

? HEPATOBILIARY ENZYMES

? ALT

- **Most specific** marker of hepatocellular injury.
- Higher in **viral hepatitis**.

? AST

- Found in heart, muscle, liver ? **less specific**.
- **AST:ALT > 2 ? alcoholic hepatitis** (very high yield).

? ALP

- Elevated mainly in **cholestasis**.
- Also high in **bone disorders**.

? GGT

- Elevated in **cholestasis + alcohol use**.
- Helps differentiate **liver ALP** from **bone ALP**.

? 5'-Nucleotidase

- **Highly specific** for cholestasis.
- Normal in bone disease.

? PANCREATIC ENZYMES

? Amylase

- Rises rapidly, normalizes in 2–4 days.
- Not specific — also ? in mumps, renal failure.

? Lipase

- **More specific** for acute pancreatitis.
- Stays elevated for up to **2 weeks**.

? MUSCLE ENZYMES

? CK-MM

- Elevated in skeletal muscle injury, rhabdomyolysis.
- Higher in Duchenne muscular dystrophy.

? Aldolase

- Elevated in **muscle diseases**, sometimes when CK is normal.

? PROSTATIC ENZYMES

? Acid Phosphatase (ACP)

- Historically used for prostate cancer.
- Now replaced by PSA.
- **TRAP** (tartrate-resistant ACP) high in **hairy cell leukemia**.

? RBC / HEMOLYSIS ENZYMES

? G6PD

- Key enzyme for NADPH.

- Deficiency causes **oxidative hemolysis** ? Heinz bodies, bite cells.
- Assay should be done **after crisis resolves** to avoid false normal.

? TUMOR MARKER ENZYMES

? Neuron Specific Enolase (NSE)

- Marker for **small cell lung carcinoma** and **neuroblastoma**.

? Placental ALP

- Elevated in **seminoma**.

? ENZYMES AS THERAPEUTIC AGENTS

- **Streptokinase, Urokinase, Alteplase (tPA)** ? thrombolysis in MI, stroke.
- **Asparaginase** ? treatment of **ALL**.
- **Pancrelipase** ? chronic pancreatitis.
- **Dornase alfa (DNase I)** ? cystic fibrosis.
- **Hyaluronidase** ? increases drug diffusion.

? IMMOBILIZED ENZYMES

- Used in **glucometers** (glucose oxidase).
- Used industrially ? **glucose isomerase** for HFCS.

- Immobilization improves **stability**, **reuse**, and **continuous operation**.

? HYPER-HIGH-YIELD PEARLS

- Troponin = best MI marker.
- CK-MB = best for reinfarction.
- Lipase > Amylase for pancreatitis.
- GGT + ALP ? = cholestasis; ALP ? + GGT normal = bone disease.
- TRAP ? = hairy cell leukemia.
- ALT > AST = viral hepatitis.
- AST > ALT = alcoholic hepatitis.
- G6PD deficiency ? oxidative hemolysis with Heinz bodies.
- NSE ? = small cell carcinoma.

? MCQs — Clinical Enzymology & Biomarkers

1. The most specific marker of myocardial infarction is:

- A. CK-MB
- B. LDH1
- C. Troponin I
- D. AST

Answer: C. Troponin I

Most sensitive and specific.

2. The earliest marker to rise in acute MI is:

- A. Troponin T
- B. LDH
- C. Myoglobin
- D. CK-MB

Answer: C. Myoglobin

3. Best marker to detect *reinfarction* is:

- A. Troponin I
- B. CK-MB
- C. LDH
- D. BNP

Answer: B. CK-MB

Falls early ? useful for recurrence.

4. “Flip pattern” (LDH1 > LDH2) is a feature of:

- A. Hepatitis
- B. Acute MI
- C. Rhabdomyolysis
- D. Renal failure

Answer: B. Acute MI

5. Most specific enzyme for liver injury is:

- A. ALP
- B. AST
- C. ALT
- D. GGT

Answer: C. ALT

6. AST:ALT ratio > 2 is characteristic of:

- A. Viral hepatitis
- B. Alcoholic hepatitis
- C. Biliary obstruction
- D. Cirrhosis

Answer: B. Alcoholic hepatitis

7. Best marker of cholestasis:

- A. ALP
- B. ALT
- C. LDH
- D. Creatine kinase

Answer: A. ALP

8. ALP is elevated in all except:

- A. Obstructive jaundice
- B. Paget disease
- C. Rickets
- D. Hemolytic anemia

Answer: D. Hemolytic anemia

9. GGT is most commonly increased in:

- A. Bone metastasis
- B. Alcohol intake
- C. Hypothyroidism
- D. Viral fever

Answer: B. Alcohol intake

10. Which enzyme differentiates liver ALP from bone ALP?

- A. LDH
- B. CK-MB
- C. GGT
- D. AST

Answer: C. GGT

11. Highly specific test for cholestasis:

- A. AST
- B. ALT
- C. γ -GT
- D. 5'-Nucleotidase

Answer: D. 5'-Nucleotidase

12. Most specific test for acute pancreatitis:

- A. Amylase
- B. Lipase
- C. LDH
- D. AST

Answer: B. Lipase

13. Amylase is elevated in all except:

- A. Acute pancreatitis
- B. Mumps
- C. Renal failure
- D. Malaria

Answer: D. Malaria

14. Elevated aldolase is seen in:

- A. Diabetes
- B. Polymyositis
- C. Hypothyroidism
- D. Viral fever

Answer: B. Polymyositis

15. TRAP (tartrate-resistant acid phosphatase) is diagnostic for:

- A. CML
- B. Hairy cell leukemia
- C. Hodgkin lymphoma
- D. Cirrhosis

Answer: B. Hairy cell leukemia

16. Enzyme replaced by PSA for prostate cancer diagnosis:

- A. ALT
- B. ACP
- C. ALP
- D. CK

Answer: B. ACP (prostatic acid phosphatase)

17. G6PD deficiency causes hemolysis due to:

- A. ATP depletion
- B. Increased 2,3-BPG
- C. Failure to regenerate NADPH
- D. Vitamin K deficiency

Answer: C. Failure to regenerate NADPH

18. In G6PD deficiency, which cells are seen on smear?

- A. Spherocytes
- B. Bite cells
- C. Auer rods
- D. Target cells

Answer: B. Bite cells

19. Tumor marker for small cell lung carcinoma:

- A. CEA
- B. AFP
- C. NSE
- D. CA-125

Answer: C. NSE (Neuron Specific Enolase)

20. Lactase is used therapeutically in:

- A. Pancreatitis
- B. Lactose intolerance
- C. Celiac disease
- D. Crohn disease

Answer: B. Lactose intolerance

21. Enzyme used in treatment of ALL (acute lymphoblastic leukemia):

- A. Streptokinase
- B. Asparaginase
- C. Urokinase
- D. Lipase

Answer: B. Asparaginase

22. Glucose isomerase is an example of:

- A. Diagnostic enzyme
- B. Therapeutic enzyme
- C. Immobilized enzyme (industrial)
- D. Fibrinolytic enzyme

Answer: C. Immobilized enzyme

23. Glucose oxidase is used in:

- A. Liver function tests
- B. Glucometers
- C. Lipid profile
- D. Tumor markers

Answer: B. Glucometers

24. Succinylcholine apnea is due to deficiency of:

- A. True cholinesterase
- B. Pseudocholinesterase
- C. LDH
- D. Lipase

Answer: B. Pseudocholinesterase

25. Dibucaine number is used to diagnose:

- A. G6PD deficiency
- B. Atypical cholinesterase
- C. Hemophilia
- D. Wilson disease

Answer: B. Atypical cholinesterase

? CLINICAL CASE-BASED QUESTIONS

1. A 54-year-old man presents with severe chest pain radiating to the left arm. ECG shows ST-elevation. Labs: Troponin I ?, CK-MB ?, LDH normal. What is the stage of MI?

Answer: Early acute MI

(Troponin & CK-MB rise early; LDH is still normal.)

2. A patient returns 3 days after MI with recurrent chest pain. Troponin is still high. Which marker will help diagnose reinfarction?

Answer: CK-MB

(Falls within 48–72 hours ? useful for detecting new infarction.)

3. A person presents 5 days after chest pain onset. Troponin and CK-MB have normalized. Which marker will still be elevated?

Answer: LDH (LDH1 > LDH2)

(Remain elevated for 7–10 days.)

4. A patient with jaundice has ALP ??, GGT ??, and 5?-nucleotidase ?. Diagnosis?

Answer: Cholestatic liver disease

(All cholestasis markers high.)

5. A child with rickets and normal GGT but high ALP. What is the origin of ALP elevation?

Answer: Bone origin

(GGT normal ? not hepatobiliary.)

6. A chronic alcoholic shows AST:ALT = 3:1 with GGT ?. What is the diagnosis?

Answer: Alcoholic liver disease

7. A patient has epigastric pain. Lipase is elevated for 10 days; amylase is normal by day 4. What condition is this?

Answer: Acute pancreatitis
(Lipase stays elevated longer.)

8. A man with chronic pancreatitis is placed on enzyme therapy. Which enzyme preparation is used?

Answer: Pancrelipase / Pancreatin

9. A boy with dark urine, pallor, and jaundice develops symptoms after taking primaquine. Blood smear shows bite cells. What enzyme deficiency is suspected?

Answer: G6PD deficiency

10. A neonate presents with severe jaundice on day 2 of life. Smear shows Heinz bodies. Most likely diagnosis?

Answer: G6PD deficiency (neonatal form)

11. After succinylcholine administration during surgery, a patient develops prolonged apnea. Which enzyme is deficient?

Answer: Pseudocholinesterase
(Diagnosed using dibucaine number.)

12. A patient with a painful swollen parotid gland has high serum amylase but normal lipase. What is the diagnosis?

Answer: Mumps (parotitis)

13. A man presents with abdominal pain. Serum amylase is high but urine amylase is low. What condition explains this?

Answer: Macroamylasemia

(Amylase binds Ig ? cannot pass into urine.)

14. A young male with easy fatigability and progressive muscle weakness has normal CK but high aldolase. What is the likely diagnosis?

Answer: Polymyositis / Dermatomyositis

(Aldolase sometimes rises when CK is normal.)

15. A 40-year-old woman has hepatosplenomegaly and bone pain. Labs show very high acid phosphatase. Suspect disease?

Answer: Gaucher disease

(RBC ACP elevated.)

16. A patient with a lytic bone lesion has very high ALP and raised ACP. What is the probable cause?

Answer: Paget disease of bone

(Osteoclast activity ? ACP ?; bone turnover ? ALP ?.)

17. A 60-year-old man with prostate cancer shows markedly elevated ACP. What other enzyme is used now for monitoring?

Answer: PSA (prostate-specific antigen)

18. A man with obstructive jaundice has elevated ALP, GGT, and bilirubin. Which enzyme pattern confirms biliary obstruction?

Answer: ALP ? + GGT ?

(Best cholestasis combination.)

19. A smoker with weight loss and cough has very high NSE levels. Most likely diagnosis?

Answer: Small cell lung carcinoma

20. A child with recurrent infections has markedly elevated LDH. Which isoenzyme pattern indicates hemolysis?

Answer: LDH1 > LDH2

(Also seen in MI, but clinical context suggests hemolysis.)

21. A patient with intense chest pain has normal troponins but elevated AST. Most likely explanation?

Answer: Skeletal muscle injury or hepatic injury

(AST alone is non-specific.)

22. A person with CF (cystic fibrosis) has thick sputum. Which enzyme therapy reduces sputum viscosity?

Answer: Dornase alfa (recombinant DNase)

23. A patient taking streptokinase shows severe bleeding. What is the mechanism of this drug?

Answer: Converts plasminogen to plasmin to fibrinolysis

24. A patient has low plasma cholinesterase but normal RBC cholinesterase. What condition is suspected?

Answer: Liver disease

(Plasma cholinesterase synthesized in liver.)

25. A patient with confusion, tremors, and high ammonia has normal bilirubin but elevated PT/INR. Which enzyme pattern supports acute liver failure?

Answer: ALT up, AST up, Cholesterol down, PT up (synthetic failure)

1. What is an enzyme marker?

A measurable enzyme in blood used to assess organ damage.

2. What makes an enzyme useful as a biomarker?

High tissue specificity, rapid release after injury, and measurable half-life.

3. Which is the most specific marker for myocardial infarction?

Troponin I / Troponin T.

4. What is the earliest marker to rise in MI?

Myoglobin.

5. Which enzyme helps detect reinfarction?

CK-MB.

6. What is the classic LDH pattern seen in late MI?

LDH1 > LDH2 ("flip pattern").

7. What are the major isoenzymes of CK?

CK-BB, CK-MB, CK-MM.

8. Which CK isoenzyme is found mainly in the heart?

CK-MB.

9. What does elevated CK-MM indicate?

Skeletal muscle injury or rhabdomyolysis.

10. Which is more specific for pancreatitis: amylase or lipase?

Lipase.

11. Why does lipase stay elevated longer than amylase?

It has a longer half-life and slower clearance.

12. What non-pancreatic condition causes elevated amylase?

Mumps (parotitis).

13. What enzyme is elevated in macroamylasemia?

Serum amylase (urine amylase is low).

14. What is the most specific liver enzyme for hepatocellular injury?

ALT (SGPT).

15. What does AST:ALT > 2 indicate?

Alcoholic liver disease.

16. What does ALP elevation indicate?

Cholestasis or bone disease.

17. How do you differentiate liver ALP from bone ALP?

Check GGT or 5?-nucleotidase.

Elevated = liver source; normal = bone source.

18. Which enzyme is specific for cholestasis?

5'-nucleotidase.

19. Why is GGT elevated in alcoholics?

Alcohol induces microsomal enzymes, increasing GGT.

20. What is TRAP?

Tartrate-resistant acid phosphatase — high in hairy cell leukemia.

21. Which enzyme is used to diagnose prostate cancer historically?

Acid phosphatase (ACP).

22. Name a tumor marker enzyme for small cell lung carcinoma.

Neuron-specific enolase (NSE).

23. What enzyme is deficient in G6PD deficiency?

Glucose-6-phosphate dehydrogenase.

24. What is the role of G6PD?

Generates NADPH for maintaining reduced glutathione.

25. Why does hemolysis occur in G6PD deficiency?

RBCs cannot handle oxidative stress ? Heinz bodies ? hemolysis.

26. What are Heinz bodies?

Denatured hemoglobin precipitates inside RBCs.

27. What are “bite cells”?

RBCs with portions removed by splenic macrophages removing Heinz bodies.

28. Name two common triggers for hemolysis in G6PD deficiency.

Primaquine and fava beans.

29. What enzyme deficiency causes prolonged apnea after succinylcholine?

Pseudocholinesterase deficiency.

30. What is the dibucaine number used for?

To detect atypical pseudocholinesterase.

31. What enzyme is used therapeutically in ALL?

L-asparaginase.

32. What enzyme is used as a thrombolytic?

Streptokinase / Alteplase (tPA).

33. Which enzyme preparation is used for chronic pancreatitis?

Pancrelipase.

34. Name an immobilized enzyme used in industry.

Glucose isomerase (for HFCS production).

35. Which enzyme is used in glucometers?

Glucose oxidase.

36. Why are immobilized enzymes useful?

Reusable, more stable, easy to separate from products.

37. What does elevated LDH5 indicate?

Liver disease or skeletal muscle injury.

38. What does elevated LDH3 suggest?

Pulmonary conditions like pneumonia or pulmonary infarction.

39. Why is troponin preferred over CK-MB?

Higher specificity and remains elevated longer.

40. What enzyme rises in rickets and Paget disease?

Bone ALP.