MEDICAL EDUCATION RESOURCE

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 + ?-ketoglutarate ? 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 **?-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

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? 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.

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

A. Troponin T

B. LDH

C. Myoglobin

D. CK-MB

Answer: C. Myoglobin

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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.

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

A. Hepatitis

B. Acute MI

C. Rhabdomyolysis

D. Renal failure

Answer: B. Acute MI

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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. ?-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 ? plasmin ? 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 ??, AST ??, Cholesterol ?, PT ? (synthetic failure)

? VIVA VOCE — Clinical Enzymology & Biomarkers

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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.

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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.