BIOCHEMICAL MARKERS

GRADE: FIRST YEAR – ASHUR MEDICAL COLLEGE 2023/2024

MODULE: SYSTEMIC / BIOCHEMISTRY

SPEAKER: DR. TAREEF FADHIL
PROFESSOR ASSISTANT & CONSULTANT PEDIATRICIAN

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OBJECTIVES

Define biochemical markers.

Identify different types of biochemical markers.

Have an introduction to cardiac biomarkers

ABBREVIATIONS

- **ALP: Alkaline Phosphatase**
- **ALT : Alanine transaminase** = serum glutamate-pyruvate transaminase (SGPT)
- **AST : Aspartate Aminotransferase** = glutamic-oxaloacetic transaminase (**SGOT :**
- **Creatine kinase : (CK), also known as creatine phosphokinase (CPK)**

Cardiac biochemical marker

1.1.B (brain type) 1.2.M (muscle type).

1.2.1.CK-MM for skeletal muscle , 1.2.2. CK-MB for cardiac muscle .

(CRP): C-reactive protein

- **GH: Growth Hormone**
- **LDH: Lactate Dehydrogenase**
- **BNP : Brain natriuretic peptide and NT-proBNP :N-Terminal pro-Brain Natriuretic Peptide**
- **HDL : (high density lipoprotein)**
- **HbA1c: Glycated Hemoglobin**
- (IL-6) : interleukin 6
- PCr: phosphocreatine.
- **T3, T4, TSH =Triiodothyronine, Thyroxine, Thyroid-Stimulating Hormone.**

BIOCHEMICAL MARKERS

Biochemical markers: These are measurable chemical indicators of a physiological process, condition, disease, or response to treatment, and they are often molecules measured through biochemical assays.
Purposes: Diagnostic, prognostic, predictive, monitoring disease progression, or assessing treatment efficacy.
Found in blood, urine, tissue, or saliva.
Types of biochemical markers: enzymes like CPK, proteins like albumin, hormones like Insulin, lipids like cholesterol, or metabolites like glucose.

TYPES OF BIOMARKERS

- **Biochemical markers.**
- **Radiological Biomarkers**
- **Molecular Biomarkers e.g.** DNA and RNA
- **Cellular Biomarkers**
- **Physiological Biomarkers**

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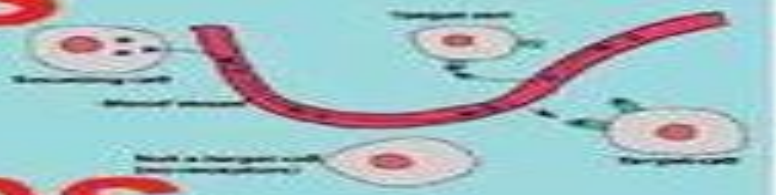
Differnces between Enzymes and Hormones





#	Hormones	Enzymes
1	They are produced from glands without any ducts(endocrine glands)	They are produced from glands having ducts (exocrine glands).
2	Chemically, they can be either proteins, steroids, polypeptides or biogenic amines.	Chemically, they are all protein in nature.
3	They are used up during a metabolic reaction.	They remain unchanged at the end of reaction (catalyst).
4	They are produced in an organ other than they perform their function i.e., they have a target organ.	They are produced in an organ where they perform their function.
5	They are easily transported through blood.	They are not transported through blood.

1-ENZYMES

Diagnostic , prognostic, predictive, monitoring disease progression, or assessing treatment efficacy.

Cardiac biochemical marker

1.1. Alanine Aminotransferase (ALT) (SGPT) and Aspartate Aminotransferase (AST)(SGOT):

Elevated ALT (SGPT) levels may indicate liver disease.

Elevated AST (SGOT) levels may indicate various medical conditions, particularly those affecting the liver, heart, or muscles.

ALT (SGOT): SGOT is included in routine blood tests, but it is not considered a primary biomarker for diagnosing or evaluating acute coronary syndromes.

- **1.2. Alkaline Phosphatase (ALP): Elevated ALP levels may indicate liver, bone disorders or rickets.**
- **1.3 Amylase: is involved in the digestion of carbohydrates.**
- **1.4. lipase is involved in the digestion of fats. Elevated blood levels of Amylase and lipase can indicate pancreatic diseases such as pancreatitis. They may be elevated in some cases of parotitis.**
- **1.5. Creatine phosphokinase (CK).**
- **1.6. Lactate Dehydrogenase (LDH).**
- **1.7. Troponins.**

2.PROTEINS

Diagnostic , prognostic, predictive, monitoring disease progression, or assessing treatment efficacy.

Cardiac biochemical marker

2.1. Myoglobin.

2.2.Albumin is a protein produced by the liver. Low levels of albumin may indicate liver disease, malnutrition, heart or kidney disease. A marker is decreased level.

2.3.Prostate-specific antigen (PSA): is a protein produced by the prostate gland. Is used as a screening test for prostate cancer.

2.4. Procalcitonin: rises especially in response to bacterial sepsis.

2.5. Acute-phase reactants are proteins whose levels in the blood increase or decrease in response to inflammation or infection:

2.5.1. C-reactive protein (CRP): Produced by the liver in response to infection, autoimmune disorders, or other inflammatory conditions.

2.5.2.Fibrinogen. Increased : Inflammation, Tissue damage/trauma, Infection coronary heart disease . **Fibrinogen (**A coagulation factor I) decreased in Hypofibrinogenemia.

2.5.3. Ferritin: Although it is more commonly used as a marker of total body iron stores.

2.5.4. D-dimer :is a fibrin degradation product present after a blood clot is degraded by fibrinolysis. It predicts thrombosis.

2.5.5. (IL-6) :used as an inflammatory marker elevated with **inflammation**, infection, autoimmune disorders, cardiovascular diseases, and some leukemias. severe COVID-19 infection with poor prognosis

3. HORMONES

Diagnostic , prognostic, predictive, monitoring disease progression, or assessing treatment efficacy.

Proteins
Amino Acid Derivative
Steroid
Cardiac biochemical marker

- 3.1. Thyroid function test : T3, T4, TSH:
- Abnormal levels of thyroid hormones or TSH can indicate thyroid disorders such as hypothyroidism or hyperthyroidism.
- 3.2. Cortisol: produced by the adrenal glands.
- 3.3. Growth Hormone (GH): Growth hormone is produced by the pituitary gland.
- 3.4. Estrogen: produced by the ovary.
- 3.5. Testosterone : produced by the testes.
- 3.6. Parathyroid Hormone (PTH) : produced by parathyroid gland.
- 3.7. Insulin: used to diagnose and differentiate diabetes type 1 &2 and monitor insulin therapy
- 3.8. Brain natriuretic peptide (BNP)and NT-proBNP (N-Terminal pro-Brain Natriuretic Peptide) (BNP)and NT-proBNP

4.LIPIDS

Diagnostic , prognostic, predictive, monitoring disease progression, or assessing treatment efficacy.

- **4.1. Cholesterol.**
- **4.2. Triglycerides.**
- **4.3. High-density Lipoproteins: HDL particles contain a higher proportion of protein relative to lipid. Referred to as "good cholesterol" because they are associated with a reduced risk of cardiovascular disease (when present in high levels) through reversing cholesterol transport, a process by which excess cholesterol is removed from peripheral tissues, including arterial walls, and transported back to the liver for excretion or recycling.**
- **4.4. low-density Lipoproteins: transport cholesterol and other lipids through the bloodstream. LDL particles are often referred to as "bad cholesterol" because high levels of LDL cholesterol in the bloodstream can lead to the formation of atherosclerotic plaques within the walls of arteries and increased risk of cardiovascular disease. Excessive levels of LDL cholesterol can lead to the accumulation of cholesterol in arterial walls.**
- **4.5. Lipid Ratios: Total Cholesterol to HDL Cholesterol Ratio High , mild or Low.**

Ratio of Total Cholesterol to HDL

Low	Mild	High
3.5	3.5-5.0	>5.0

Ratio of Cholesterol

		Optimal	Moderate	High
Total/HDL ratio	Men	<3.5	3.5 – 5.0	>5.0
	Women	<3.0	3.0 - 4.4	>4.4
LDL to HDL ratio		<2.5	2.5 – 3.3	>3.3
HDL to LDL ratio		>0.4	0.4 to 0.3	<0.3
TG to HDL ratio		<2	2 – 3.8	>3.8

Units: mg%

	Desirable	Borderline High	High
Total Cholesterol	Less than 200	200 - 239	240 and higher
LDL Cholesterol (the "bad" cholesterol)	Less than 130	130 - 159	160 and higher
HDL Cholesterol (the "good" cholesterol)	50 and higher	40 - 49	Less than 40
Triglycerides	Less than 200	200 - 399	400 and higher

QUIS 1 :

- You are measuring a patient's cholesterol and HDL levels. Total cholesterol level is (100+ **?**) mg%, and HDL levels = 45. **? = your registration #**

1-Obtain **Total Cholesterol to HDL Cholesterol Ratio.**

2- Classify the Result into optimal, moderate, or high.

5. CARBOHYDRATES

Diagnostic , prognostic, predictive, monitoring disease progression, or assessing treatment efficacy.

- 5.1. **Glucose**.
- **5.2.Glycated Hemoglobin (HbA1c).**
- **5.3. Lactate:** a marker of tissue hypoxia or metabolic acidosis.

6- ELECTROLYTES

Diagnostic , prognostic, predictive, monitoring disease progression, or assessing treatment efficacy.

- **6.1. S. Sodium (Na+): hypernatremia,** Hyponatremia.
- **6.2. S. Potassium (K+): hyperkalemia :** > 5.5 mEq/L (> 5.5 mmol/L), usually caused by **renal failure, medications,** or **acidosis. Hypokalemia= Deceased leveles**
- **6.3. S. Chloride (Cl-). Increased levels = hyperchloremia, and decreased = hypochloremia.**
- **6.4. S. Calcium (Ca2+). Hypocalcemia vs hypercalcemia.**
- **6.5. mg+2 : hypomagnesemia vs hypermagnesemia (**kidney failure or is treatment-induced e.g. from antacids that contain magnesium)
- **In general abnormal electrolyte levels can indicate various medical conditions, including dehydration, kidney disorders, endocrine disorders, heart problems, and electrolyte imbalances caused by medications or other factors.**

List of biomarkers in COVID-19 classified according to organ/system involved.

	Neutrophilia
	Depletion of CD4+ and CD8+ cells
	Elevated neutrophil-to-lymphocyte ratio (NLR)
	Thrombocytopenia/thrombocytosis
Inflammation	Cytokines
	Chemokines
	Growth factors
	C reactive protein
	Procalcitonin
	Lactate dehydrogenase
Coagulation	D-dimer levels
	Fibrinogen
	Fibrin degradation products (FDP)
	Prothrombin time (PT)
	Activated partial thromboplastin time (aPTT)
Cardiac	Cardiac troponin (ctn)
	Brain natriuretic peptide (BNP)/NT-proBNP
Hepatic	Aspartate aminotransferase (AST)
	Alanine aminotransferase (ALT)
	Bilirubin
	Albumin
Muscle	Creatine-kinase (CK)
	Myoglobin
Renal	Serum creatinine
Electrolytes	Hyponatremia
	Hypokalemia
	Hypocalcemia

NOT ALL BIOMARKERS ARE BIOCHEMICAL MARKERS

CPK

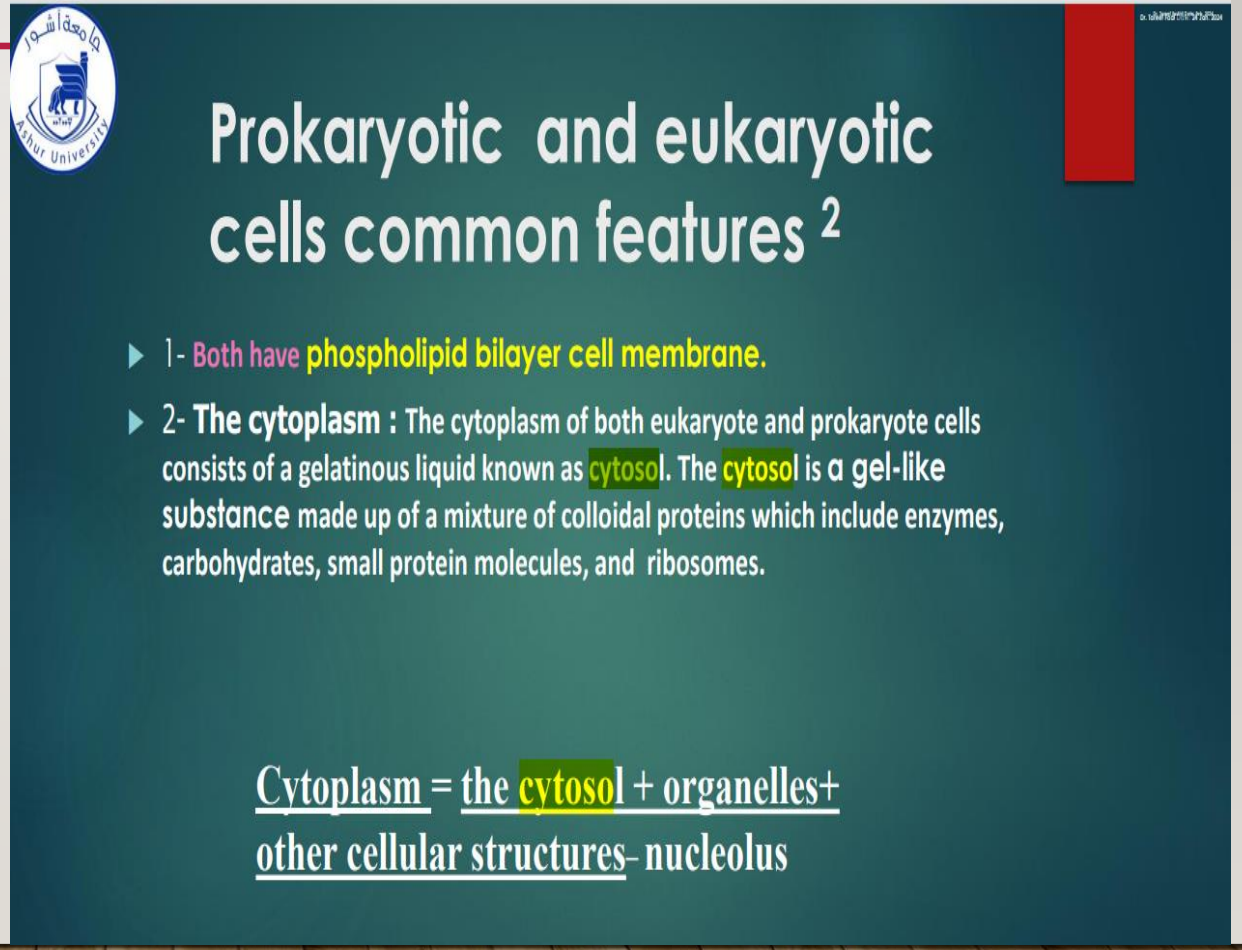
- **Creatine kinase (CK), also known as creatine phosphokinase (CPK), is an enzyme found in three cytosolic CK isoforms, there are two mitochondrial CK isoenzymes. :1. cytosolic and 2. mitochondrial forms.**

The term *cytosol* is used to refer to the liquid phase of the cytoplasm. This excludes any part of the cytoplasm that is contained within organelles.

Creatine kinase (CK)

- Three main CK isoenzymes with two polypeptide chains B or M

1.The "cytosolic" CK enzymes :
1.1.B (brain type) 1.2.M (muscle type).
1.2.1.CK-MM, 1.2.2. CK-MB.
2.Mitochondreial CK enzymes:
2.1.Ubiquitous mitochondrial creatine kinase (uMtCK).
2.2. Sarcomeric mitochondrial creatine kinase (sMtCK).



1.The “cytosolic” CK enzymes

Cytosolic creatine kinase (CK) is a key enzyme involved in cellular energy metabolism, especially in tissues with high and fluctuating energy demands.

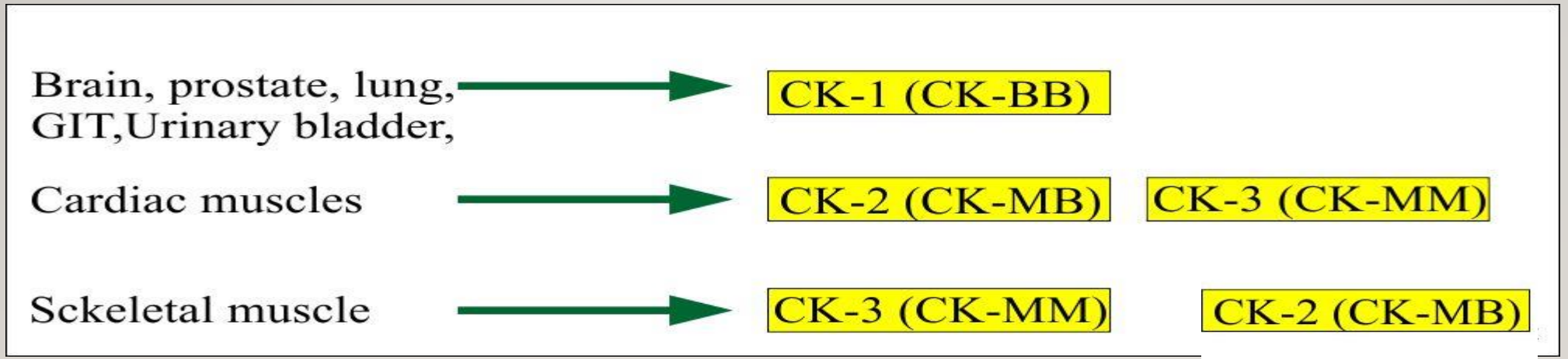
1.The “cytosolic” CK enzymes :

1.1.CK-BB (Brain type):

- This isoform is predominantly found in tissues such as the brain, and smooth muscle. This includes the smooth muscles of various organs such as the **GIT, genital tracts**, and blood vessels.

- **CK-BB forms very small quantities of total CK and is normally undetectable in blood.**
- **1.2.M (muscle type) :2 isoenzymes: 1.2.1.CK-MM, 1.2.2. CK-MB.**
- **1.2.1.CK-MM**
- **95 % of total CK.**
- **CK-MM 98% in skeletal muscle (SM) & 2% in cardiac muscle (CM)**
- **1.2.2. CK-MB**
- **CK-MB: less than 5 % of total CK.**
- **CK-MB: 90% in CM&10% in SM .**

	% of total CK	Distribution of isoenzyme	Causes of elevation
1.1.CK-BB	normally undetectable in blood	95% of CK activity in the brain	Tends to rise in a brain injury, meningitis, abnormal cell growth, severe shock, stroke, hypothermia, or restricted blood flow to the bowel.
1.2.1. CK-MM	95 % of total CK.	98% in skeletal Muscle (SM) & 2% in cardiac muscle (CM	Rises damage in skeleton after a crush injury, seizures, muscular dystrophy, muscle inflammation, or another skeletal muscle disorder. Damage in heart .
1.2.2. CK-MB	less than 5 %	90% in CM&10% in SM .	Cardiac ischemia . Skeletal muscle injury can sometimes cause elevated CK-MB levels.


Brain, prostate, lung,
GIT,Urinary bladder,
CK-1 (CK-BB)
Cardiac muscles
CK-2 (CK-MB)
CK-3 (CK-MM)
Sckeletal muscle
CK-3 (CK-MM)
CK-2 (CK-MB)

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Total creatine phosophokinase (CPK)

ase

hart Junpaparp, MD; Chief Editor: Eric B Staros, MD more...

Reference Range

Normal findings

Total creatine phosophokinase (CPK) [1] :

Adult/elderly:

- Male: 55-170 units/L or 55-170 units/L (SI units)
- Female: 30-135 units/L or 30-135 units/L (SI units)

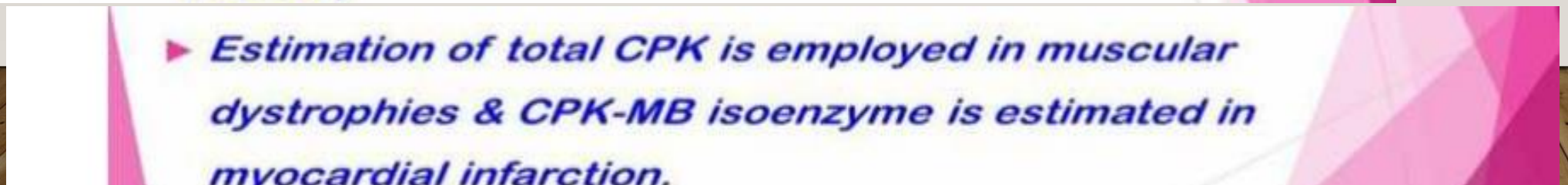
(Values are higher following exercise.)

Newborn: 68-580 units/L (SI units) [1]

Isoenzymes [1] :

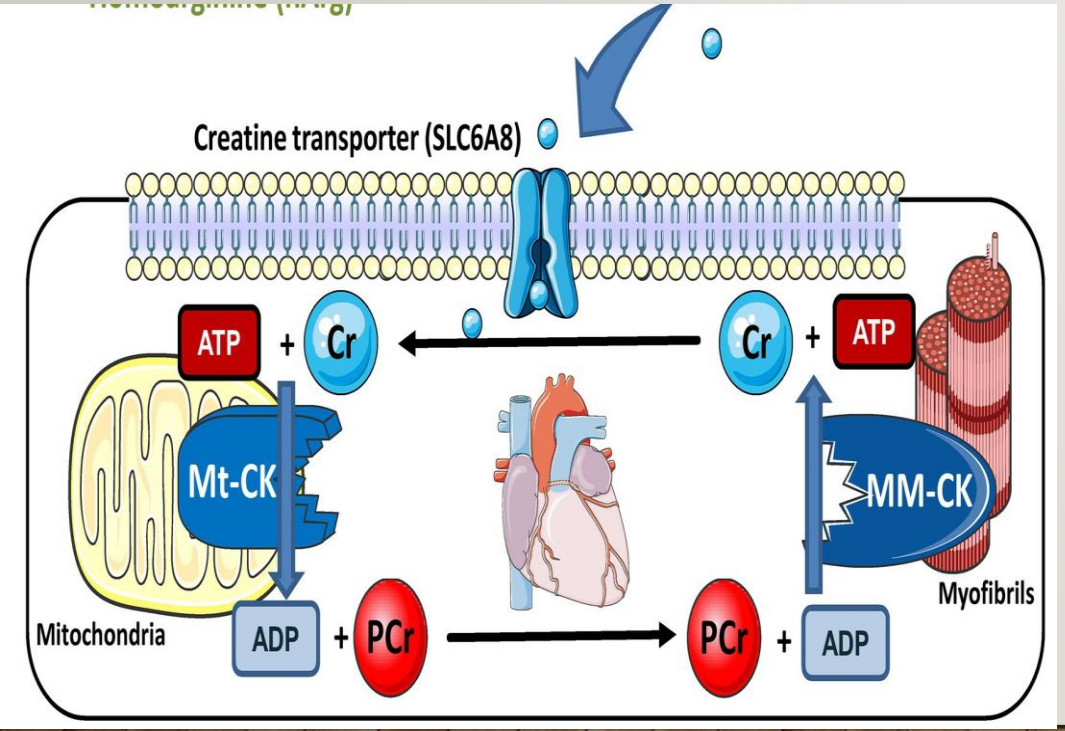
Serum Total CK elevation is not specific. Increased in cardiac and in a variety of non-cardiac conditions (false positive result) like; trauma, intramuscular injection, skeletal muscle breakdown (Rhabdomyolysis), muscle dystrophy.





2.MITOCHONDREIAL CK ENZYMES:
2.1.UBIQUITOUS MITOCHONDRIAL CREATINE KINASE (UMTCK).
2.2. SARCOMERIC MITOCHONDRIAL CREATINE KINASE (SMTCK).

- While mitochondrial CK is directly involved in formation of phosphocreatine (PCr) from mitochondrial ATP, cytosolic CK regenerates ATP from ADP, using PCr.
- This happens at intracellular sites where ATP is used in the cell, with CK acting as an in situ ATP regenerator.



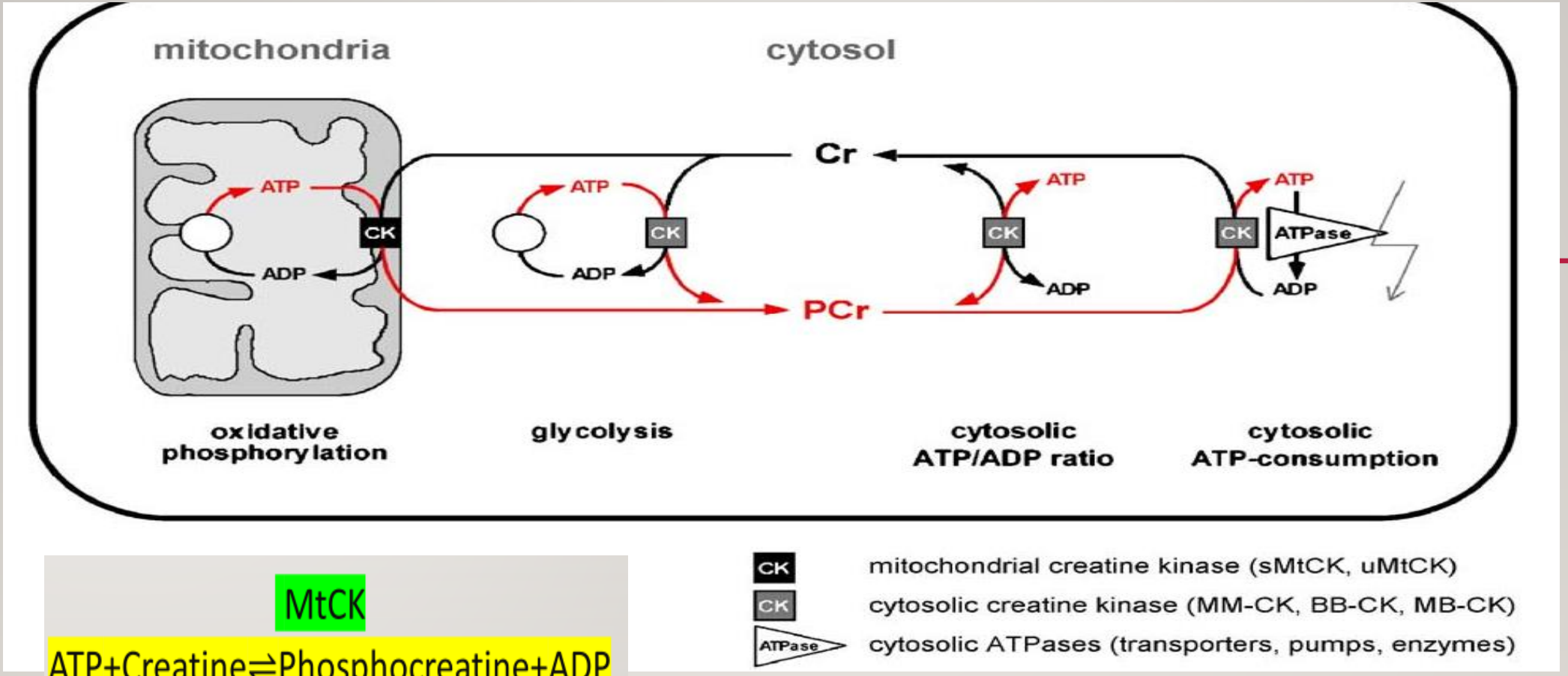
CK/PCr circuit or shuttle

Mitochondrial CK (CK_m)

ATP+Creatine⇌Phosphocreatine+ADP

cytosolic CK

ADP+Phosphocreatine⇌ATP+Creatine



MtCK

ATP+Creatine⇌Phosphocreatine+ADP

cytosolic CK

ADP+Phosphocreatine⇌ATP+Creatine

Mitochondrial creatine kinase (CK_m) regenerates phosphocreatine (PCr) from mitochondrially generated ATP and creatine (Cr) imported from the cytosol.

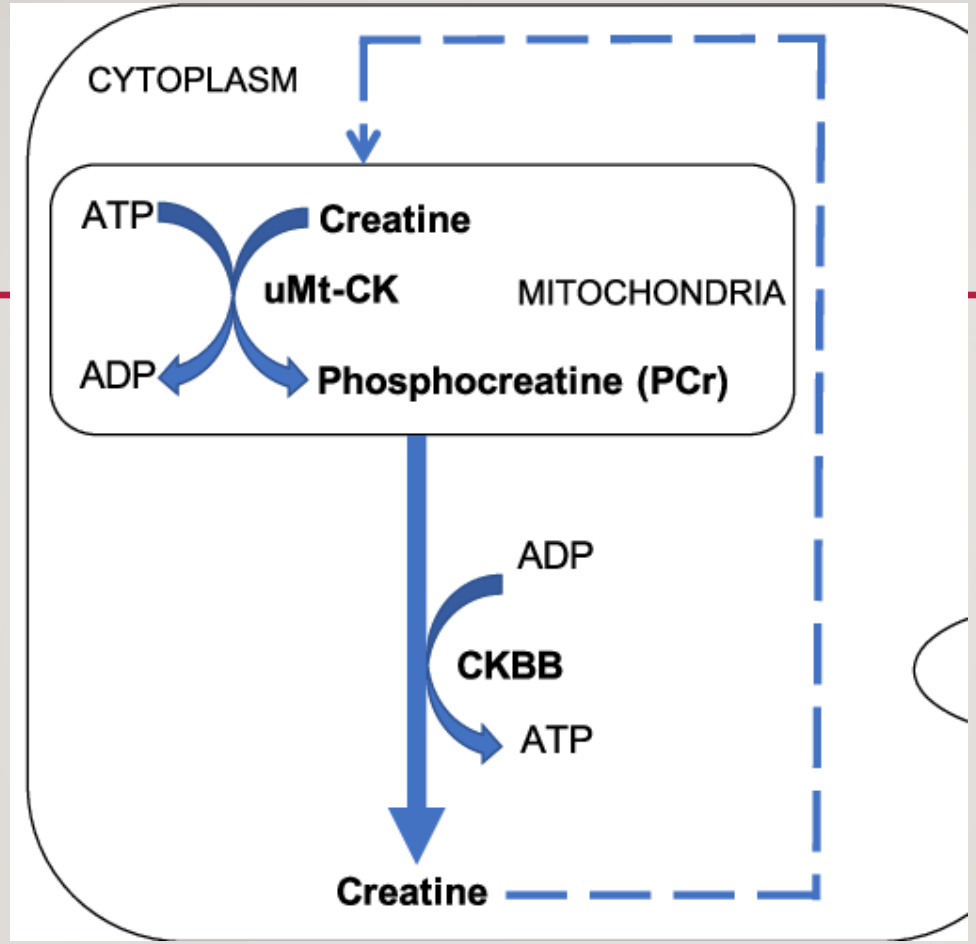
CK/PCr circuit or shuttle

MtCK

ATP+Creatine⇌Phosphocreatine+ADP

cytosolic CK

ADP+Phosphocreatine⇌ATP+Creatine

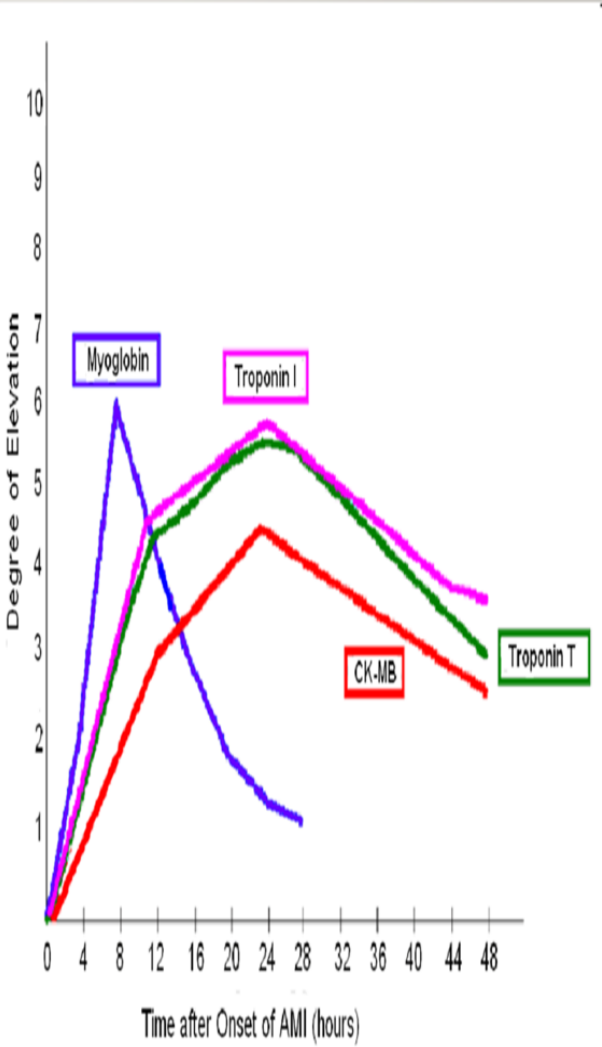


CK/PCr circuit or shuttle

CARDIAC BIOCHEMICAL MARKERS

- Are substances that are released into the bloodstream in response to heart damage .
- They are often used in clinical practice to diagnose and monitor various cardiac conditions, e.g. :
- Ischemic heart disease.
- heart failure.
- Commonly used cardiac biomarkers:
- 1-Creatine Kinase-MB (CK-MB).
- 2- Troponins.
- 3- Myoglobin.
- 4- Brain Natriuretic Peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP).
- 5- Lactate Dehydrogenase (LDH).
- 6- SGOT (AST)

Marker	Detection onset (post MI) (hrs.)	range	Peak (post MI) (hrs.)	Return to Normal	Sensitivity (%)	Specificity (%)
CPK-MB	4-6	<6U/L	12-24	48 – 72 (hrs.)	50-70%	85-90%
CK-MB ratio		<3				
Troponin I	2-4	<0.08 ug/L	12 to 24	5 -10 days	90-95	90-95
Troponin T				5-14 days		
Myoglobulin	1 - 3	15-120 <0.08 ug/L	6 to 12	24 (hrs.)	70-90	40-60
LDH	12 - 24	40 - 280 (IU/L)	48 - 72	longest Days - weeks	40-60	60-70
SGOT (AST)	4-6		24-48	5 - 7 days	High	low
					AST/ALT ratio of 0.63 high sensitivity and specificity	



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Thank You