

Biochemistry
Team 434

Biochemical Markers of Myocardial Infarction

Biochemistry434@gmail.com

Objectives:

- Myocardial infarction
- Time-course of plasma enzyme changes
- Cardiac troponins I and T
- Creatine kinase (CK-MB)
- Myoglobin

Color Index:

- **Important**
- **Explanation**
- **Females slides**
- Extra Notes

Abbreviations:

CK=Creatine Kinase
Hrs=Hours
MI=Myocardial infarction
CHF=Congestive Heart Failure

○ Myocardial infarction is due to:

- Occlusion of coronary arteries → leads to blockage of the artery.
- Restricted blood supply (oxygen) to heart tissue (**ischemia**) →
- Damage to heart tissue (**infarction**) →
- Release of enzymes and other proteins into the blood (**markers**)

AMI : Gross necrosis of the myocardium as a result of interruption of the blood supply to an area of cardiac muscle .
Cardiac marker: a clinical laboratory test useful in cardiac disease , most commonly for detecting AMI or myocardial injury . If markers are found in the blood (high amount) that is an up-normal condition.

○ Diagnosis of MI

:Recommended by the European Society of Cardiology and American College of Cardiology

- Requires presence of at least two of the following characteristics:
 1. Typical heart attack symptoms.
 2. Characteristic rise and fall pattern of a cardiac marker in plasma.
 - Rise and gradual fall of cardiac troponins.
 - More rapid rise and fall of creatine kinase MB.
 3. Typical ECG pattern.

○ Features of an ideal cardiac marker

- Should be present in high concentration in the myocardium.(so once the heart is damaged it can release it).
- Absence from non-myocardial tissue,(only present in heart).
- High sensitivity(you can detect it), and specificity.
- Rapid release into plasma following myocardial injury.
- Correlation between plasma level and extent of myocardial injury for prognosis.(more damage > higher release).
- Detectable by rapid, simple and automated assay methods.

The ideal marker in myocardial injury would persist in circulation for several days to provide a late diagnostic time window for patient who arrived late after the event .

The **CARDIAC TROPONINS** meet these criteria .

○ Plasma MI markers

- **OBSOLETE MARKERS**
 - Aspartate Transaminase(AST)(not used anymore).
 - Lactate dehydrogenase (LDH) and its isoenzymes. (not used anymore).
- **CURRENT MARKERS**
 - **Creatine kinase (CK) and CK-MB**
 - **Troponin T**
 - **Troponin I**
 - **Myoglobin**
- **MARKERS UNDER ASSESSMENT (with potential for clinical use):**Might be used in the future, but not used right now.
 - CK-MB isoforms.
 - High sensitivity c-reactive protein (CRP)
 - B-type natriuretic peptide.

○ Markers of diagnostic value in MI:

Cardiac troponins T and I
Creatine kinase (CK-MB)
Myoglobin
B-type natriuretic peptide

Blood samples collected after MI:

Baseline (upon admission)

Between 12 and 24 hours after the onset of symptoms.

○ Time-course of plasma enzyme changes

- Plasma enzymes follow a pattern of activities after MI.
- The initial lag phase lasts for about 3 hours.
- Enzymes rise rapidly to peak levels in 18-36 hours.
- The levels return to normal based on enzyme half-life.
- Rapid rise and fall indicates diagnostic value.

○ Troponins

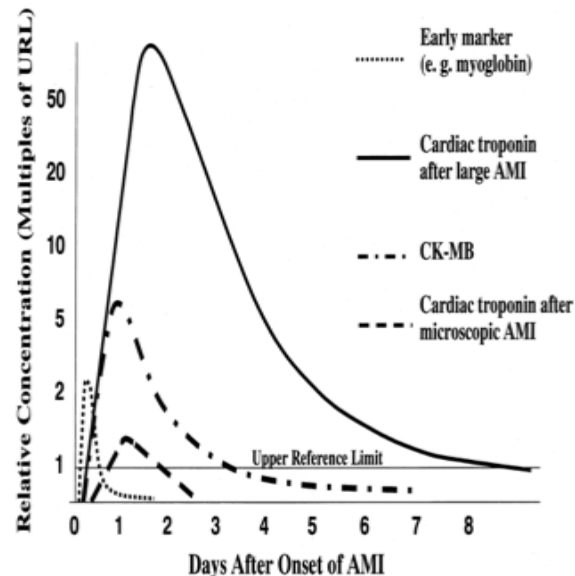
- Troponins are structural proteins in cardiac myocytes and in skeletal muscle.
- Involved in the interaction between actin and myosin for contraction.
- cTn are mainly bound to proteins, with small amount soluble in the cytosol.
- Two main cardiac troponins (cTn):
cTnI: inhibitory protein
cTnT: binds to tropomyosin

Troponins are highly specific.

-After a MI, cytosolic troponins (soluble) are released rapidly into the blood (first few hours). usually after 3hrs.

-Structurally bound troponins (insoluble) are released later for several days which account for the prolonged plateau of troponin release.

Under normal circumstances there is no cardiac troponin T or I detectable in blood .



Creatine Kinase

Definition..?

Three main CK isoenzymes* with 2 polypeptide chains B or M.
Second specific marker, After troponin.

Type	Composition			Comment
	MM	MB	BB	
Skeletal Muscle	98%	2%		Elevated in muscle disease
Cardiac muscle	70-80%	20-30%		Cardiac muscle has highest amount of CK-MB
Brain**			√	
Plasma**	√			

*Differ in amino acid sequence but catalyze the same chemical reaction.

**B with BB, M with MM.

1. CK-MB characteristics:

More sensitive and **specific** for MI than total CK

It rises and falls transiently after MI

Appears in blood within 4-6 hrs of heart attack
-Peak **12-24 hrs**

Returns to normal within 2-3 days

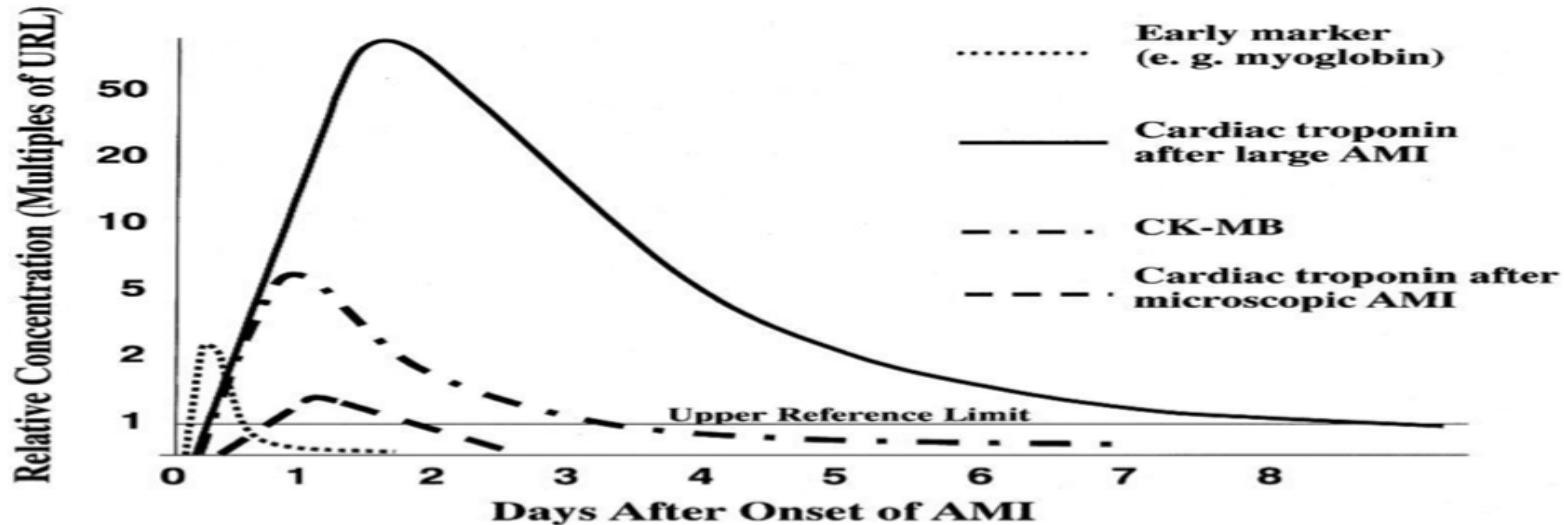
Relative index = $\text{CK-MB mass} / \text{Total CK} \times 100$
Relative index > 5% indicates MI

2. Advantages vs Disadvantages

Advantages	Disadvantages
Useful for early diagnosis of MI	Not significant if measured after 2 days of MI (delayed admission)
Useful for diagnosis of re-infarction (2nd infarction)	Not highly specific (elevated in skeletal muscle damage)

MI marker changes in plasma

Enzyme / Protein	Detectable (hours)	Peak value (hours)	Duration (days)
CK-MB	3-10	12-24	1.5-3
Total CK	5-12	18-30	2-5
Cardiac troponins	3-4	12-24	upto 10



MYOGLOBIN

- Myoglobin is a sensitive marker of cardiac damage.
 - Appears in blood earlier than other markers (within 1-4 hours).
- It rises very rapidly after the MI at about the same rate as CK-MB.
- It is non-specific because it is elevated in:
 - Muscle disease/injury
 - Acute and chronic renal failure

B-type natriuretic peptide (BNP)

Definition..?

-A peptide hormone produced by the **ventricles** of the heart.

In response to..?

-Myocardial stretching and ventricular dysfunction.

It causes..?

1. Vasodilation
2. Na and H₂O excretion and reduces blood pressure.

It is used for..?

-Diagnosis of (**CHF**).

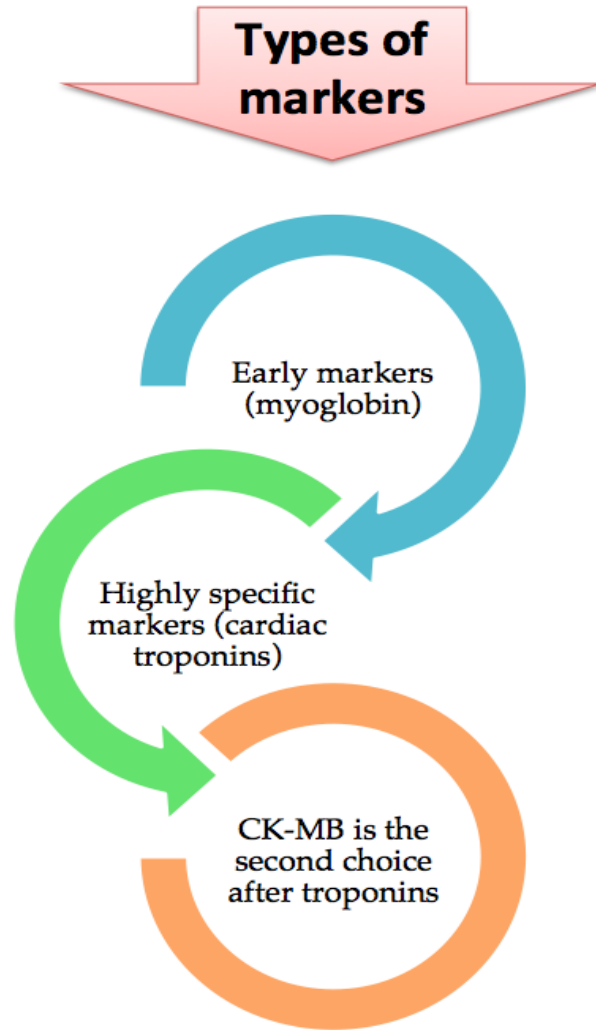
Half life time:

Has a short half life (20 minutes).

It is highly specific and sensitive but we can't detect it because of the short half life.

MI Marker Recommendations

- Measurement of plasma MI markers
Upon admission of patient and **serially** thereafter.
- Use of fast and robust test methods for
marker detection



Diagnosis of AMI

- Recommended by the European Society of Cardiology and American College of Cardiology
- Requires presence of at least **two** of the following characteristics:
 1. Ischemic symptoms
 2. Typical rise and fall pattern of a cardiac marker in plasma
 - a. Typical rise and gradual fall of cardiac troponins **or**
 - b. More rapid rise and fall of CK- MB
 3. Typical ECG pattern(changes)
- It was rare for a diagnosis of AMI to be made in the absence biochemical evidence of myocardial injury .
- The guidelines recognized the reality that **neither** the clinical presentation **nor** the ECG had adequate sensitivity and specificity .
- This guideline does not suggest that all increase of these biomarkers should elicit a diagnosis of AMI, **only those associated with the appropriate clinical and /or ECG findings.**

CASE

66 yr old man had experienced central chest pain on exertion for some months , but afternoon of the day prior to admission he had a severe episode of pain ,

Which come on without any exertion and lasted for about one hour .

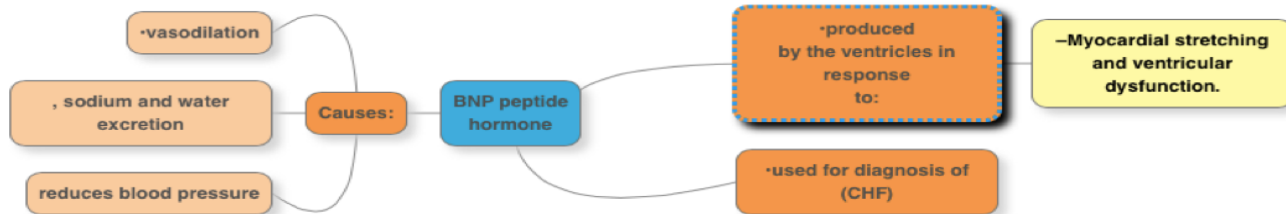
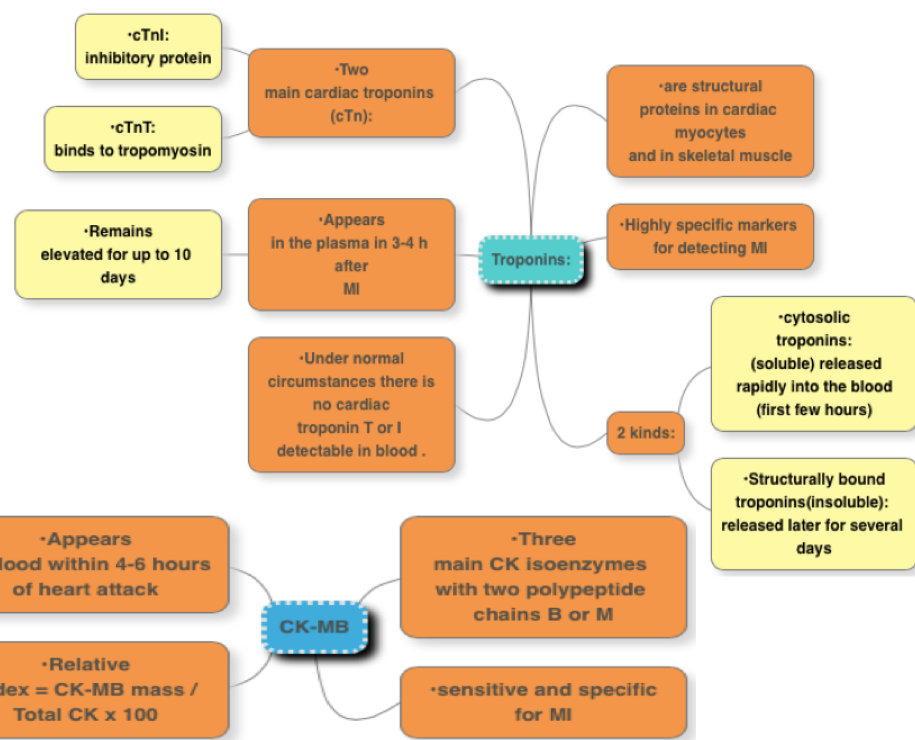
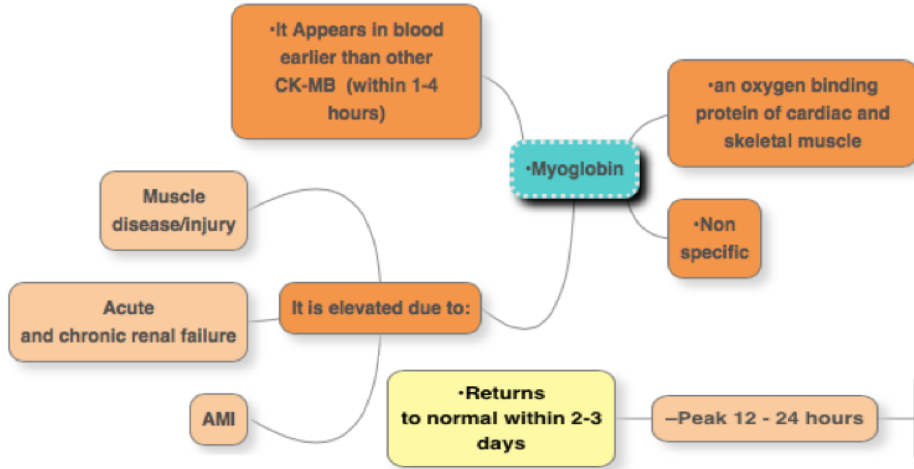
On admission there were no abnormalities on examination and ECG was normal. Tn was clearly detectable .

Has he suffered a myocardial infarction???

MOST COMMON IN HIS CASE:

- He has an elevated troponin plus a typical history .
- This is sufficient to diagnose a MI by the most recent definition , even in the absence of ECG changes

Summary:



MCQs:

check your understanding

1-IDEAL CARDIAC MARKER SHOULD HAVE:

- A.-LOW CONCENTRATION IN THE MYOCARDIUM BUT ABSENCE IN OTHER TISSUE
- B.-HIGH CONCENTRATION IN THE MYOCARDIUM AND LOW CONCENTRATION IN OTHER TISSUE
- C.-HIGH CONCENTRATION IN THE MYOCARDIUM AND ABSENCE IN OTHER TISSUES

2-WHICH ONE OF THE CARDIAC MARKERS ITS PLASMA LEVEL CAN DETERMINE THE SEVERITY OF THE CARDIAC DAMAGE?

- A.-CK-MB
- B.-TROPONIN
- C.-MYOGLOBIN

3-WHICH ONE OF THE CARDIAC MARKERS IS A STRUCTURAL PROTEIN?

- A.B-TYPE NATRIURETIC PEPTIDE
- B.CK-MB
- C.TROPONIN

4- TROPONIN AND CK-MB ARE BOTH FOUND IN CARDIAC AND SKELETAL MUSCLES, WHAT MAKES TROPONIN MORE SPECIFIC FOR CARDIAC DAMAGE?

- A.CK-MB IS NOT RELEASED AFTER SKELETAL MUSCLE DAMAGE
- B.CARDIAC T_n ARE STRUCTURALLY DIFFERENT FROM SKELETAL MUSCLES TROPONIN
- C.TROPONIN IS NOT MORE SPECIFIC

5-AFTER 6 DAYS OF A MYOCARDIAL INFARCTION, WHICH ONE OF THE CARDIAC MARKERS YOU CAN DETECT?

- A.TROPONIN
- B.MYOGLOBIN
- C.CK-MB

6-A 73 YEARS OLD MALE CAME TO ER COMPLAINING FROM SEVERE CRUSHING SUB-STERNAL CHEST PAIN, A BLOOD SAMPLE WAS TAKEN IMMEDIATELY AND REVEALED NO ELEVATION IN CARDIAC ENZYMES, WHAT WILL YOU DO?

- A.GIVE HIM MORPHINE AND LET HIM GO HOME
- B.TAKE ANOTHER BLOOD SAMPLE AFTER HOURS
- C. WAIT FOR X-RAY IF IT IS FINE LET HIM GO HOME

7-THE FIRST CARDIAC MARKERS CAN BE DETECTED IS?

- A.MYOGLOBIN
- B.TROPONIN
- C.CK-MB

8-A 62 YEARS OLD DIABETIC PATIENT CAME TO THE HOSPITAL, HIS CLINICAL HISTORY REVEALED THAT HE HAD HEARTBURN (ACID REFLEX) A 9 DAYS AGO,

HIS BLOOD SAMPLE SHOWS ELEVATION OF TROPONIN AND CK-MB, WHAT IS YOUR INTERPRETATION?

- A.GASTROESOPHAGEAL REFLUX DISEASE (GERD)
- B.HIATAL HERNIA
- C.RE-INFARCTION



CHECK OUT THIS VIDEO YOU MAY FIND IT HELPFUL:

<https://www.youtube.com/watch?v=rKVGv9F74GE>

Answers:

1-C

2-B

3-C

4-B

5-A

6-B

7-A

8-C

Done by:

Sara alsalman

Reema alrasheed

Rasha bassas

Reema alhammad

Mohammed alotaibi

Mohammed almashouq

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