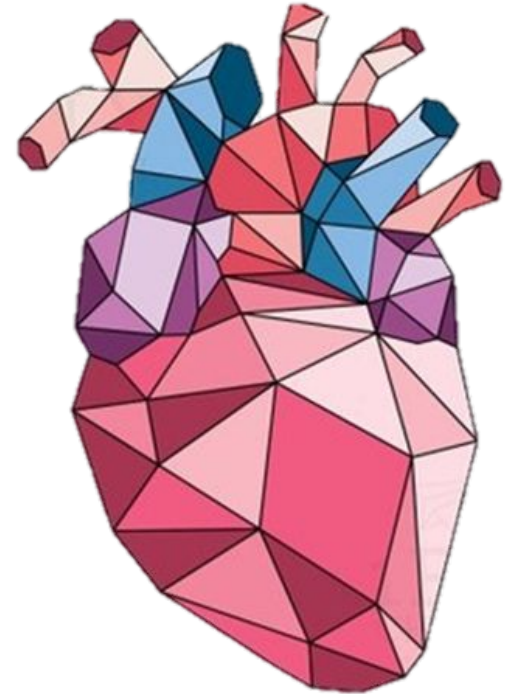




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# Biochemical Markers Of Myocardial Infarction












## Color Index:

- **Original content**
- **Important**
- Extra info, Dr's notes

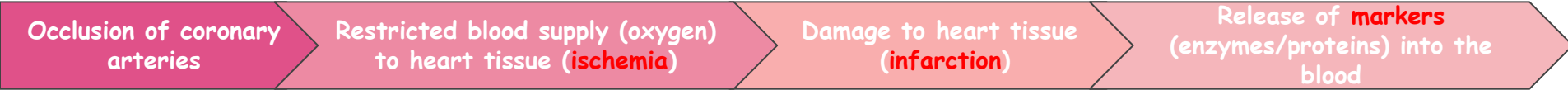
## Objectives:

- Slide No. 3  Describe the general sequence of events of myocardial infarction (MI)
- Slide No. 3  List the criteria for diagnosis of MI
- Slide No. 4  Discuss the features of an ideal MI marker
- Slide No. 6  Understand the significance of changes in plasma marker levels over time
- Slides (7-10)  Identify the properties and diagnostic value of cardiac troponins, creatine kinase, h-FABP and BNP
- Slide No. 5  Know about markers with potential clinical use

## Overview:

-  Myocardial infarction (MI)
-  Criteria for diagnosis of MI
-  Case example for MI
-  Features of an ideal MI marker
-  Time-course of plasma enzyme changes
-  Cardiac troponins I and T
-  Creatine kinase (CK-MB)
-  Heart fatty acid binding protein (h-FABP)
-  B-type natriuretic peptide (BNP)

# Myocardial Infarction (MI)



- ★ These markers are natural components in the myocytes (intracellular). they're not supposed to be found in the blood like  $\text{Na}^+$  or  $\text{K}^+$  so if a blood test indicate their presence this suggests the death of some myocytes (**myocardial infarction**)

## Criteria For Diagnosis Of MI

- Recommended by the european society of cardiology and american college of cardiology
- Requires the presence of **At least 2** of the following characteristics :

### 1 Typical heart attack symptoms

e.g. chest pain , shortness of breath .. etc

### 2 Characteristic Pattern of a cardiac marker in the plasma

- Rise and gradual fall of cardiac **troponins**
- More rapid rise and fall of **CK-MB**

### 3 Typical ECG pattern

e.g. elevated ST segment


## case:

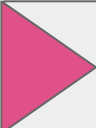
A 66 year-old man had experienced central chest pain on exertion for some months, but in the afternoon of the day prior to admission he had a particularly severe episode of the pain, which came on without any exertion and lasted for about an hour. On admission there were no abnormalities on examination and the ECG was normal. The troponin was clearly detectable.

### Comments:

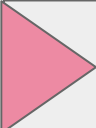
1. ↑ Troponin (Characteristics pattern of a cardiac biomarker)
  2. Typical heart attack symptoms
- 2 characteristics = myocardial infarction**  
(in the most recent definition even in the absence of ECG changes)

# Features Of An Ideal Cardiac Marker


 High concentration in the myocardium

 High sensitivity

Detected even in low concentration at early stages of the disease

 High specificity

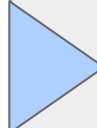
Specifically detecting damage of cardiac tissue, and absent in other tissue injury

 Rapid release into plasma following myocardial injury

 **Good prognostic value**

strong correlation between plasma level and extent of myocardial injury

★ E.g. ↑ Troponin = ↑ Myocardial injury

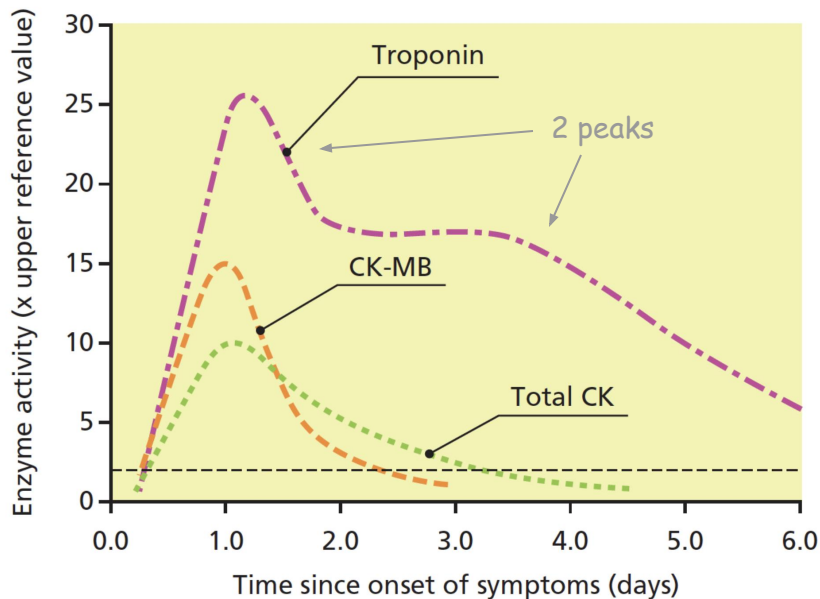
 Easily measured

detectable by rapid, simple and automated assay methods

# Plasma Cardiac Markers

Current MI Marker	Markers with potential clinical use	Markers no longer used (low specificity)
Cardiac troponin T (cTnT)	Heart fatty acid binding protein (h-FABP)  * detecting heart tissue ischemia	Aspartate Transaminase (AST)
Cardiac troponin I (cTnI)		Lactate Dehydrogenase (LDH)
Creatine kinase-MB (CK-MB) <small>Myocardium Bound</small>		Ischemia modified albumin (IMA)
		Myoglobin

# Time-Course Of Plasma Enzyme Changes



	Abnormal activity detectable (h)	Peak value of abnormality (h)	Duration of abnormality (days)
Troponin T or I	4-6	12-24	3-10
CK-MB isoenzyme	3-10	12-24	1.5-3
Total CK	5-12	18-30	2-5



Total CK is used for the ratio between CK- MB and CK. (discussed later)

- ★ 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

## Blood samples collected after MI:

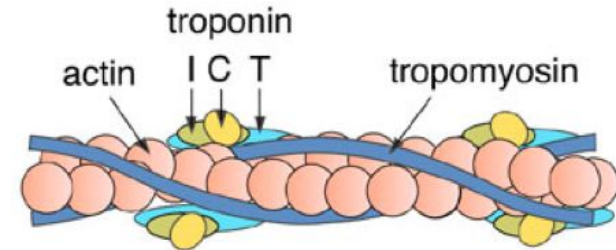
- Baseline (upon admission)
- Between 12 and 24 hours after the onset of symptoms

# Troponins

structural proteins in cardiac myocytes and in skeletal muscle

## Cardiac Troponins (cTn)

Structure	Structurally different from muscle troponins	
Function	Involved in the interaction between actin and myosin for muscle contraction	
Location	<b>Bound to proteins (Mainly)</b> <ul style="list-style-type: none"><li>Released later</li><li>Several days</li><li>Causes the second peak</li></ul>	<b>soluble in the cytosol (small amount)</b> <ul style="list-style-type: none"><li>Released rapidly into the blood after MI</li><li>first few hours</li><li>Causes the first peak</li></ul>
Importance	Highly specific markers for detecting MI	
Types	<b>cTnI</b> Inhibitory protein	<b>cTnI</b> binds to Tropomyosin



# Creatine Kinase (CK)

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

Type	Composition	Comment
Skeletal Muscle	98% CK-MM 2% CK-MB	Elevated in muscle disease
Cardiac muscle	70-80% CK-MM 20-30% CK-MB	has highest amount of CK-MB
Brain	CK-BB	-
Plasma	Mainly CK-MM	CK is found in the plasma when it's released from cells. So, since CK-MM is the major component of most cells (cardiac & skeletal) plasma will mainly contain CK-MM



# CK-MB

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

Rises and falls transiently after MI

Advantages	Disadvantages
<p>Useful for <b>early diagnosis of MI</b> (because its released to blood earlier than troponin.)</p>	<p>Not significant if measured <u>after 2 days</u> of MI (delayed admission)</p>
<p>Useful for diagnosis of <b>re-infarction</b> (after 3 days of MI CK-MB would disappear while troponin will be low. So if we detect elevated CK-MB and low troponin it means a second episode of MI)</p>	<p>Not highly specific (<b>elevated in skeletal muscle damage</b>)</p>

## Relative index

$$\text{CK-MB mass} / \text{Total CK} \times 100$$

More than **5 %** is indicative for MI

## Heart Fatty Acid Binding Protein (h-FABP) (Heart tissue ischemia marker)

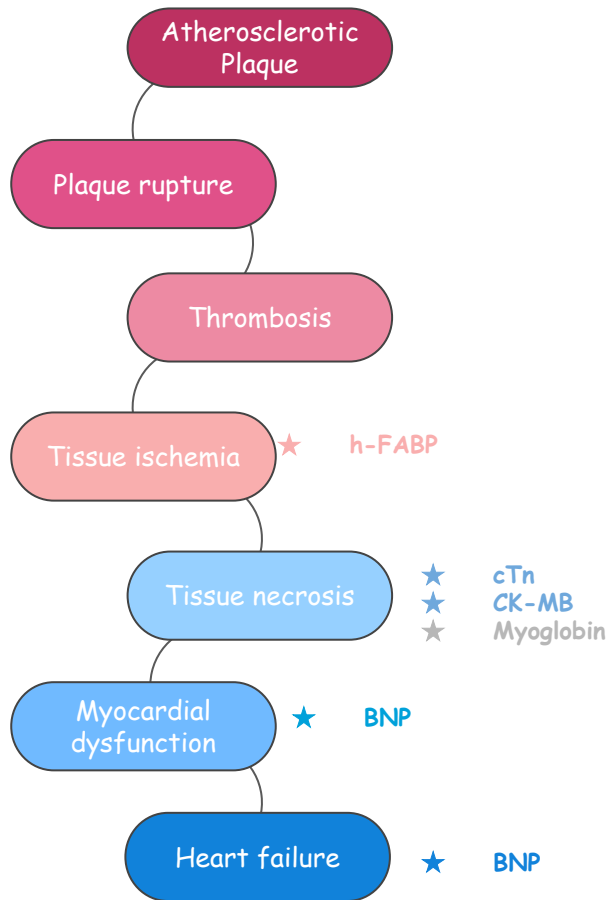
Definition	<ul style="list-style-type: none"> <li>A cytosolic protein involved in fatty acid transport and metabolism.</li> <li>It's a promising marker to be used in <b>combination with troponins</b>.</li> </ul>
Existing	Higher amounts in myocardium than in brain, kidney & skeletal muscle.
Appearance	<ul style="list-style-type: none"> <li>Appears in plasma as early as <b>30 min.</b> after acute <b>ischemia</b>. <small>(early detection of MI)</small></li> <li>Peaks in blood in <b>6-8 h.</b> <small>Due to rapid renal clearance of this marker.</small></li> <li>Returns to normal levels in <b>24-30 h.</b></li> </ul>

## B-Type Natriuretic Peptide (BNP) (heart failure marker)

Definition	A peptide produced by the ventricles of the heart in response to myocardial stretching & ventricular dysfunction <b>after MI</b> .
It causes	<ol style="list-style-type: none"> <li>Vasodilation</li> <li>Sodium and water excretion</li> <li>Reduction in blood pressure</li> </ol>
Marker for	<b>Detecting congestive heart failure.</b>
Facts	<ul style="list-style-type: none"> <li>Its serum levels are high in some pulmonary diseases whilst in heart failure its levels are markedly high. <small>(used to differentiate between pulmonary disease &amp; heart failure)</small></li> <li>An important marker for differential diagnosis of pulmonary diseases and congestive heart failure.</li> </ul>

# Pathogenesis Of MI

" with special focus on the biomarkers implicated in the development of MI "



## case:

A well-trained marathon runner collapsed as he was approaching the finishing line. An ECG was normal but CK was elevated at 9500 U/L (reference range 30-200 UL) , and the CK - MB was 14 % of the total CK (normally <6%). Troponin was undetectable .

### Comments:

The total CK is substantially elevated and CK - MB > 6 % can usually be taken to mean that it is of myocardial origin. However, the normal ECG and troponin are both reassuring. In trained endurance athletes, the proportion of CK-MB in muscle increases from the normal low levels and may be as high as 10-15 % . An elevated CK - MB in such individuals can no longer be taken to imply a cardiac origin for the raised CK. **Extreme exercise, especially in unfit individuals, causes an elevated CK, potentially to very high levels.**

# Take home message



## cTn

- Currently the most definitive markers and are replacing CK-MB
- Highly specific to heart muscle damage
- They remain elevated in plasma longer than CK-MB
- They have higher sensitivity and specificity than CK-MB



## CK-MB

Its main advantage is for detecting re-infarction



## h-FABP

An early marker for detecting acute ischemia prior to necrosis



## BNP

A cardiac marker that can be used for differential diagnosis of pulmonary diseases and heart failure

# Quiz

## MCQs

**Q1:** which one of the following below is an indicator of myocardial infarction?

- a) Sodium                      b) Troponin                      c) calcium                      d) potassium

**Q2:** Troponin appears in the blood within?

- a) 12-24 h                      b) 4-6 h                      c) 3-10 h                      d) 6-12 h

**Q3:** which of the following is used in early detection of MI

- a) Troponin                      b) CK-MB                      c) BNP                      d) h-FABP

**Q4:** cardiac muscle has the highest amount of

- a) CK-MM                      b) CK-MB                      c) CK-BB                      d) B&C are equal

**Q5:** Marker for differential diagnosis of pulmonary diseases & congestive heart failure?

- a) CK-MB                      b) cTnT                      c) BNP                      d) h-FABP

**Q6:** h-FABP returns to Normal level in:

- a) 30 min                      b) 6-8 h                      c) 1.5-3 days                      d) 24-30 h

## SAQs

**Q1:** Give 3 features of an ideal cardiac marker.

**Q2:** List the advantages and disadvantages of CK-MB

**Q3:** A recently retired lawyer was admitted to the hospital with chest pain that had developed during the evening after a day spent digging in the garden.

No specific signs on the ECG. Lab tests reports are below, what is your diagnosis? :

- CK(total) = 300 U/L (normal range= 30-200U/L)
- CK-MB index = 1.6% (normal percentage= 0-4%)
- Troponin T = 0.03 $\mu$ g/L (normal range= 0.0 - 0.01 $\mu$ g/L)

**Q4:** how long has this patient been diseased (in question 3)

★ **MCQs Answer key:**

- 1) B      2) B      3) B      4) B      5) C      6) D

★ **SAQs Answer key:**

- 1) - High concentration in the myocardium  
- High sensitivity  
- High specificity  
- Rapid release into plasma following myocardial injury  
- Good prognostic value  
- Easily measured
- 2) \* Advantages early diagnosis of MI, diagnosis of re-infarction  
\* Disadvantages:  
- Not significant if measured after 2 days of MI  
- Not highly specific (elevated in skeletal muscle damage)
- 3) Myocardial infarction
- 4) Since CK-MB/CK = 1.6% (normal) and troponin is slightly high most likely that MI occurred more than 3 days ago

## Team members

### Girls team :

- Ajeed Al-rashoud
- Alwateen Albalawi
- Elaf Almusahel
- Haifa Alessa
- ★ Lama Alassiri
- ★ Lina Alosaimi
- ★ Nouf Alhumaidhi
- Noura Alturki
- ★ Nouran Arnous
- Reem Algarni
- Shahd Alsalamh
- Taif Alotaibi

### Boys team :

- Abdullah Altuwaijri
- Alkaseem binobaid
- Fares Aldokhayel
- Naif Alsolais
- Sultan Alhammad

## Team leaders

Deema Almaziad

Mohannad Alqarni

WORK HARD IN SILENCE, LET THE  
SUCCESS MAKE THE NOISE

