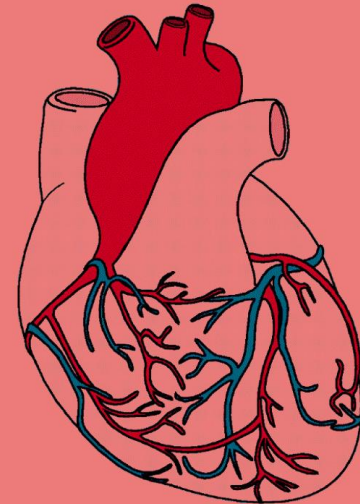


# Biochemical Markers of Myocardial Infarction



Color index :






Main text

**IMPORTANT**

Extra Info

Drs Notes

## Objectives:

-  Describe the general sequence of events of myocardial infarction (MI)
-  List the criteria for diagnosis of MI
-  Discuss the features of an ideal MI marker
-  Understand the significance of changes in plasma marker levels over time
-  Identify the properties and diagnostic value of cardiac troponins, creatine kinase, h-FABP and BNP Know about markers with potential clinical use

# Myocardial infarction (MI)

[Learn more about Myocardial infarction, or skip to 7:00](#)



Occlusion of coronary arteries.

Eg. in case of atherosclerosis, which is a disease characterized by plaque builds up inside the arteries.



Restricted blood supply (which is carrying oxygen) to heart tissue “**ischemia**”.

As we know when the perfusion is reduced (as in case of atherosclerosis), ischemia will develop.



Damage to heart tissue “**infarction**”.

Prolong ischemia leads to infarction.



Release of enzymes and other proteins into the blood “**markers**”.

After tissues death, natural components in the myocytes will be released in the blood (eg. Cardiac troponin T & I, Creatine kinase-MB), so if we did a blood test and found even a small amount of these component, that's will be an indicator for MI and the patient should be hospitalized.

## Criteria For 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:

“check (case 1) in slide NO.12 for better understanding”

**A**

Rise and fall pattern of a cardiac marker in plasma:

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

**B**

Typical heart attack symptoms.

can be taken from the patient's history.  
E.g.: chest pain, shortness of breath, tightness of the jaws.

**C**

Typical ECG pattern.

- might be absent.
- E.g. elevated ST segment.



# Features Of An Ideal Cardiac Marker

1

## High concentration in the myocardium.

- Troponin can be found in the myocardium in a high concentration.

2

## High sensitivity:

- detected even in **low concentration** at early stages of the disease.

3

## High specificity:

- specifically detecting **damage of cardiac tissue**, and is **absent in non-myocardial tissue injury**.
- E.g : patient with acute pancreatitis will not have troponin in his blood, because it's only specific for heart diseases.
- Dr: for example high AST doesn't indicate damage of a cardiac tissue

4

## Rapid release into plasma following myocardial injury.

- This feature help in early detection of the damage due to Rapid release of the markers after the damage.

5

## Good prognostic value:

- strong correlation between plasma level and extent of myocardial injury.
- I.e : **severe** myocardial injury = high level of troponin, **less severe** myocardial injury = lower level of troponin.

6

## Easily measured:

- why do we want it to be easily measured? because we usually need it in an emergency situations.
- detectable by rapid, simple and automated assay methods.

# Plasma cardiac markers

## CURRENT markers of diagnostic value in MI

1- Cardiac troponin **T** (cTn**T**) "protein"

2- Cardiac troponin **I** (cTn**I**) "protein"

3- Creatine kinase-MB (CK-MB) "enzyme"

## Markers with POTENTIAL CLINICAL USE

### Markers of diagnostic value in TISSUE ISCHEMIA :

1- Heart fatty acid binding protein (h-FABP)

## Markers of diagnostic value in HEART FAILURE

1- B-type natriuretic peptide (BNP)

## Markers NO LONGER USED

1- Aspartate Transaminase (AST)

2- Lactate dehydrogenase (LDH)

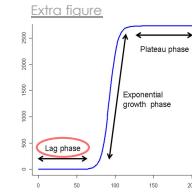
3- Ischemia modified albumin (IMA)

4- Myoglobin

These markers are not used for heart diseases any more, why ?  
they're highly non-specific for the heart diseases, instead they're specific in other organs diseases. E.g. : AST is more specific in liver diseases than the heart diseases.  
And just to refresh your memory,  
#Foundation : ALT is more specific than AST in liver diseases

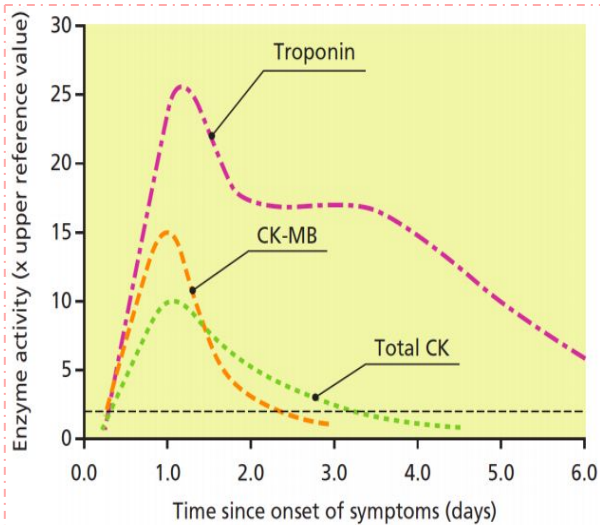
# Time-course of plasma enzyme changes

- Plasma enzymes follow a pattern of activities after MI.
- The initial **lag phase** lasts for about **3 hours** at this time the rise is undetectable.
- (Lag phase : duration between the damage and releasing the markers "the time that the marker takes to be detectable "
- Enzymes rise rapidly to **peak levels** in **18-36 hours** BUT keep in mind each marker will have a different pattern.
- The levels **return to normal** based on **enzyme half-life**.
- Rapid rise and fall** indicates diagnostic value.
- Troponin**: Rapid rise because it is more sensitive and because there is many unbound troponin in the cytoplasm that will get out in the plasma very fast and gradual fall. **CK-MB**: Rapid rise and fall. "Look at the figure below"



## Blood samples collected after MI:

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



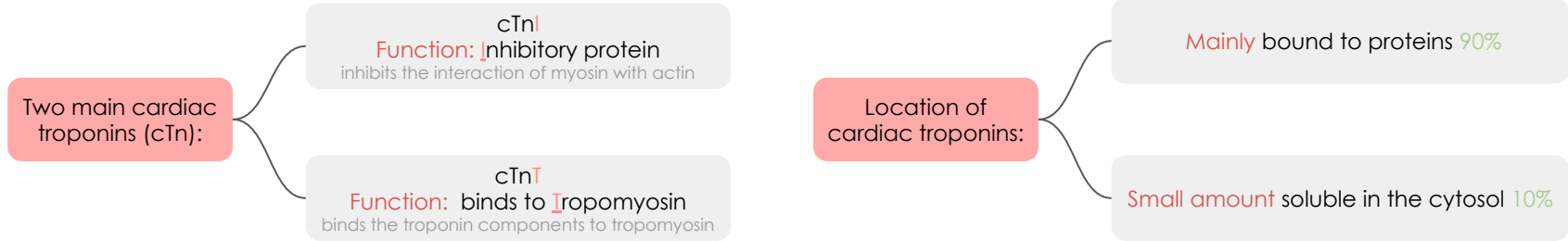
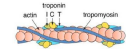
★ Time-course of plasma biochemical marker elevation after changes after MI  
 " each will be discussed in details "

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

# 1) Troponins

Unlike other cardiac biomarker troponin is not an enzyme it is a protein

- Troponins are structural proteins in **cardiac myocytes** and in **skeletal muscle**.
- However, **Cardiac troponins** (cTn) are structurally different from **muscle troponins**.
- There are 3 subunit of Troponin (I, T, C), each one of these subunit is slightly different between cardiac and skeletal Troponins.
- Involved in the interaction between actin and myosin for muscle contraction.
- ★ **Highly specific markers for detecting MI.**



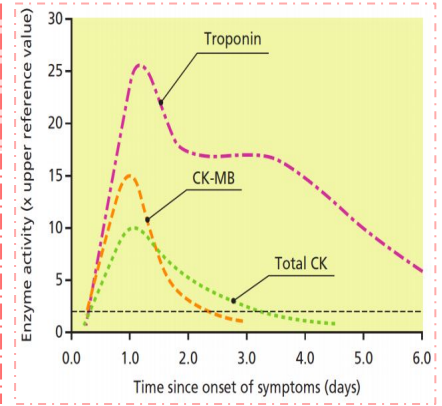
Enzyme	Abnormal activity detectable in plasma after:	Peak value of abnormality	Duration of abnormality
Troponin T or I	4-6 h	12-24 h	up to 10 days

- **Cytosolic troponins** (10% of cTn in the cytosol) : are released rapidly into the blood (first few hours)

- **Structurally bound troponins** (90% of cTn bound to proteins) : are released later for several days

- Because we have a small amount soluble in the cytosol, troponin is highly detectable at the beginning. And it doesn't drop completely after 1.5-3 days (like CK-MB) because the structurally bound troponin will be release in the blood after days from releasing the cytosolic troponins.

**That's why troponin lasts for a long time.**



# Creatine kinase (CK)

- ▶ Creatine kinase (CK) occurs as three isoenzymes.
- ▶ isoenzymes : two or more enzymes with **identical function** but **different structure**.
- ▶ Each isoenzyme is a dimer composed of two polypeptides (called B and M subunits) associated in one of three combinations: CK1 = BB, CK2 = MB, and CK3 = MM.

Type	Composition	Comment
Cardiac muscle	70-80% CK-MM 20-30% CK-MB	Cardiac muscle has highest amount of CK-MB
Skeletal Muscle	98% CK-MM 2% CK-MB	Elevated in muscle disease
Brain	CK-BB	Useful tool in the diagnosis and prognosis of the brain diseases
Plasma	Mainly CK-MM	-



- CK-MB is specific but not as specific as troponin.  
- as you can see CK-MB can be found in both Cardiac and Skeletal muscle.



## 2) CK-MB

➤ **CK-MB** is **more sensitive** and **specific** for MI than **total CK**.

➤ It rises and falls transiently **after MI**.

"check (case 2) in slide NO.12 for better understanding"

➤ **Relative index** =  $\frac{\text{CK-MB mass}}{\text{Total CK} \times 100}$  , More than **5 %** is indicative for MI

### Advantages

- Useful for **early** diagnosis of MI.

the CK-MB has risen more than the total CK Because CK-MB is more sensitive and specific for MI than total CK

- ★ Useful for diagnosis of **re-infarction**.

Because unlike troponin, CK-MB goes back to normal after 1.5-3 days

#MED436 It is expected for a MI patient to have **recurrent MI**.

Because troponin can be present in blood for 10 days, then we can't tell if the patient had another MI or not. But because the CK-MB falls within 3 days, we can detect that it fell down and re-raised again which tells us that the patient had another MI.

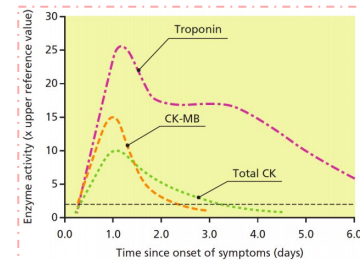
### Disadvantages

- **Not** significant if measured after 2 days of MI (delayed admission).

in this case we can measure **troponin** to know if he had an infarction

- **Not** highly specific (elevated in skeletal muscle damage)

Enzyme	Abnormal activity detectable in plasma after:	Peak value of abnormality	Duration of abnormality
<b>CK-MB isoenzyme</b>	<b>3-10 h</b>	<b>12-24 h</b>	<b>1.5-3 days</b>

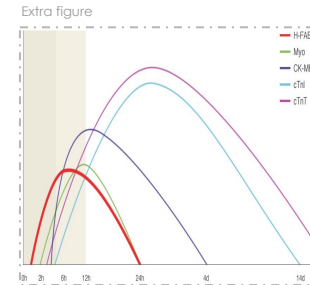


### 3) Heart fatty acid binding protein (h-FABP), is a Heart tissue ischemia marker

- ▶ A cytosolic protein involved in fatty acid transport and metabolism.
- ▶ A promising marker to be used in **combination** with troponins.
- ▶ Site: Higher amounts in myocardium than in brain, kidney and skeletal muscle.
- ★ Used for: **Heart tissue ischemia**, i.e. early stage of MI

Detect ischemia before infarction.  
Help in detect MI before necrosis  
#Med435

Enzyme	Abnormal activity detectable in plasma after:	Peak value of abnormality	Duration of abnormality
★ <b>h-FABP</b>	<b>30 min</b> after acute ischemia	<b>6-8 h</b>	<b>24-30 h</b>

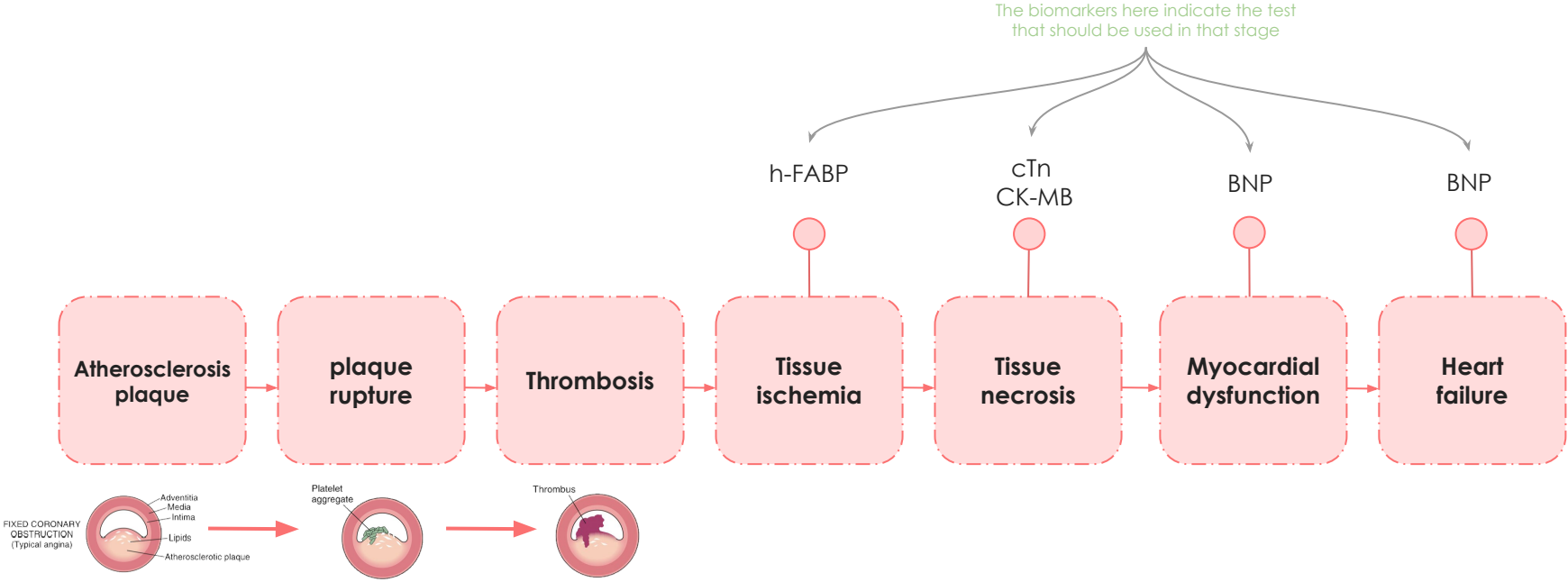


### 4) B-type natriuretic peptide (BNP), is a Heart failure marker

- ▶ A peptide **produced by the ventricles of the heart in response to:**
  - Myocardial stretching and ventricular dysfunction **after MI**.
- ▶ It will **cause** :
  - vasodilation.
  - sodium and water excretion.
  - reduces blood pressure.
- ★ A marker for detecting: **congestive heart failure**.
- ▶ Its serum levels are high in some **pulmonary diseases**. But in **heart failure** its levels are **markedly** high.
- ▶ An **important marker for differential diagnosis of:** pulmonary diseases and congestive heart failure.

# Pathogenesis of MI :

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



## Case 1

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 had a particularly severe episode of the pain, which came on without any exertion and lasted for about an hour.<sup>(1)</sup> On admission there were no abnormalities on examination and the ECG was normal. The troponin was clearly detectable<sup>(2)</sup>.

### Comments:

- 1) Typical heart attack symptoms
- 2) Characteristic Pattern of Cardiac biomarker

He has an elevated troponin & a typical history. **This is sufficient to diagnose a myocardial infarction** by the most recent definition, **even in the absence of ECG changes.**

## Case 2





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 U/L), and the CK-MB was 14% of the total CK (normally less than 6%). Troponin was undetectable "normal" .

### Comments:


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

# Take Home Messages

## cTn

-  Currently the most definitive markers and are replacing CK-MB.
-  Highly specific to heart muscle damage (**MI**).
-  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

Q1 : Troponin lasts in the blood for ..... days, and CK-MB for ..... days .

- |            |            |            |           |
|------------|------------|------------|-----------|
| A ) 10 , 5 | B ) 10 , 3 | C ) 3 , 10 | D ) 5 , 3 |
|------------|------------|------------|-----------|

Q2 : Which one of following biomarkers is used to detect ischemia ?

- |            |              |           |         |
|------------|--------------|-----------|---------|
| A ) h-FABP | B ) Total CK | C ) CK-MB | D ) BNP |
|------------|--------------|-----------|---------|

Q3 : Which one of following biomarkers is used to detect CHF ?

- |            |              |           |         |
|------------|--------------|-----------|---------|
| A ) h-FABP | B ) Total CK | C ) CK-MB | D ) BNP |
|------------|--------------|-----------|---------|

Q4 : Which one of following biomarkers is the MOST sensitive and specific to MI?

- |              |              |           |            |
|--------------|--------------|-----------|------------|
| A ) Troponin | B ) Total CK | C ) CK-MB | D ) IDK :) |
|--------------|--------------|-----------|------------|

Q5 : Which one of following biomarkers is used to detect re-infarction?

- |              |           |         |           |
|--------------|-----------|---------|-----------|
| A ) total-CK | B ) CK-MM | C ) BNP | D ) CK-MB |
|--------------|-----------|---------|-----------|

Q6 : biochemistry team is :

- |                        |       |                        |                                   |
|------------------------|-------|------------------------|-----------------------------------|
| A ) The BEST team ever | B ) A | C ) for sure it's A !! | D ) you're still thinking<br>😞😞!! |
|------------------------|-------|------------------------|-----------------------------------|

## SAQs :

Q1: list 3 features of an ideal cardiac marker

Q2: list the advantages and disadvantages for using CK-MB in diagnosing MI

Q3: Mention the locations of troponin ? and the releasing time of each ?

★ MCQs Answer key:

1) B    2) A    3) D    4) A    5) D    6) A

★ SAQs Answer key:

1) High sensitivity, specificity, and high concentration in myocardium

2) check **slide 9**

3)

- **cytosolic troponins** : released rapidly (first few hours)
- **Structurally bound troponins** : released later for several days

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Noura Alshathri  
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Abdullah Alanzan  
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Abdullaziz Alrabiah

 Abdulaziz Alsalem



☆ Special thanks to **Manal Altwaim** for her amazing work and efforts

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