

# Biochemical markers of myocardial infarction

“Do something today that your future self will thank you for”

## Objectives:

- Recall the criteria for diagnosis of myocardial infarction (MI).
- Know about the features of an ideal MI marker.
- Understand the significance of plasma marker changes over time.
- Identify properties and diagnostic value of MI markers such as cardiac troponins, creatine kinase and myoglobin.
- Be familiar with some of the new markers.

### Color index:

- **Important**
- Extra explanation

\* Please check out [this link](#) to know if there are any changes or additions.

# Cardiac Markers:

<b>What are they?</b>	A clinical laboratory test (a test which is taken in the washroom) useful in cardiac disease, most commonly for detecting AMI or myocardial Injury.
<b>Features of an Ideal cardiac marker:</b>	<b>1- High concentrations in the myocardium.</b>
	<b>2- High specificity</b> – specifically detecting damage of cardiac tissue, and <b>is absent in non-myocardial tissue injury.</b> يعني فقط يدلنا على الامراض القلبية ، ما يدلنا على أمراض الكبد والقلب والعضلات مع بعض فنضطر نجري إختبارات أخرى علشان نعرف مسبب المرض.
	<b>3- Rapid Release into plasma following myocardial Injury.</b> هذي الخاصية بتساعدنا بتشخيص مبكر للمرض ، فمن تحدث الانجري على طول يروح للبلازما ماينتظر ايام أو أسابيع.
	<b>4- Good prognostic value</b> – strong correlation between blood level and extent of myocardial injury for prognosis. أيضا من خصائص الماركر الجيد إذا كانت فيه علاقة واضحة بين نسبته بالدم وشدة المرض ، فمثلا نسبة التروبونن العالية دليل على شدة المايوكارديال انفراكشن
	<b>5- High sensitivity</b> – detectable even <u>in low concentration</u> at early stages of the disease.
	<b>6-Easily measured</b> – detectable by rapid, simple and automated assay methods.
	<b>7- Persist in the circulation for several days</b> , to provide a late diagnostic time window for patient who arrived late after the event. موب كل الناس بيستيجبون للمرض بنفس الطريقة ، البعض يروح للطواريء على زكمه خفيفه والبعض يتحمل آلام وما يجي إلا وهو خالص ، فكيف ممكن نشخص المرض إذا جانا متأخر؟ لازم يكون عندنا ماركر يطول بالسركليشن

# Myocardial Infraction:

<b>Due to</b>	<b>Occlusion of coronary arteries → Ischemia (restricted blood supply to heart tissues) → Infraction (damage to heart tissues) → Release of markers (proteins and other enzymes) into the blood.</b>	
<b>AMI (Acute Myocardial Infraction):</b>	Gross necrosis of the myocardium as a result of interruption of the blood supply to an area of cardiac muscle.	
<b>Biomarkers of MI in plasma</b>	<b>Obsolete Markers</b> <i>(they're highly not specific for the heart, so they're not used anymore)</i>	Aspartate Transaminase (AST)
		Lactate dehydrogenase (LDH)
	<b>Current cardiac markers (troponins, CK-MB and myoglobin are</b>	Troponins (I or T)
		Creatine kinase-MB (CK-MB)
Myoglobin		

	<p>markers of <b>diagnostic value in MI</b>, while hFABP is a marker of <b>diagnostic value in tissue ischemia</b>)</p>	<p>-Markers with potential clinical use:-</p> <p>Heart fatty acid binding protein (hFABP) (for tissue ischemia).</p> <p>New marker, Detect ischemia before infarction. Help in detect MI before necrosis</p>
Blood samples collected after MI:	<ul style="list-style-type: none"> <li>- Baseline (upon admission)</li> <li>- Between 12 and 24 hours after the onset of symptoms</li> </ul>	

## Myocardial Infraction markers:

### 1- Troponins: "Highly specific marker for detecting MI"

What are troponins?	<p>- Troponins are structural <b>proteins</b> in <b>cardiac myocytes</b> and in <b>skeletal muscle</b>, which are Highly specific markers for detecting MI. t Involved in the interaction between <b>actin and myosin</b> for contraction.</p> <p>(Cardiac troponins (cTn) are structurally different from muscle troponins).</p>
Location:	cTns are mainly bound to proteins (insoluble), with small amount soluble in the cytosol
main cardiac troponins (cTns):	<p><b>cTnI</b> → <b>inhibitory protein</b></p> <p><b>cTnT</b> → <b>binds to tropomyosin</b></p>
Appear in plasma:	<b>3-4 h after MI</b>
Remain elevated for:	<b>Remain elevated for up to 10 days</b>
useful in:	useful in <b>excluding AMI after 12 h following chest pain</b> or other symptoms
Prolonged troponin plateau:	<p>After a MI:</p> <ul style="list-style-type: none"> <li>- <b>(first few hours): cytosolic</b> troponins (soluble) are released rapidly into the blood.</li> <li>- <b>(Later for several days): Structurally bound</b> troponins (insoluble) are released later for several days which account for the prolonged plateau of troponin release.</li> </ul> <p>التروبونين يقعد في الجسم تقريبا لمدة ١٠ أيام .. لكن ياترى ماسبب هذه المدة الطويلة؟  كما ذكرنا في بداية الجدول أن التروبونين متواجد في مكانين:  - الكمية الأقل في السيترول (مذابه – ماتحتاج أحد يساعدها علشان تتحرك) .  - الكمية الأكبر غير مذابة ومرتبطة بالبروتينات (علشانها غير مذابه فتساعدها بالحركة "نفس فكرة اللايوبروتينز").</p>

عند حدوث المايوكارديال انفراكتشن، في الساعات الأولى الكمية الموجودة في السيترول راح تطلع للدم ، أما الكمية المرتبطة بالبروتين فيتطلع خلال أيام "نقدر نقول لأنها ثقيلة".

## Creatine kinase (CK)

### CK isoenzymes:

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	Cardiac muscle has highest amount of CK-MB
Brain	CK-BB	-
Plasma	Mainly CK-MM	-

## 2- Creatine Kinase-MB (CK-MB):

Facts:	CK-MB is more sensitive and specific for MI than total CK
	It rises and falls transiently after MI
Appears In:	Appears in blood within <b>3-10 hours of heart attack</b>
Peaks in blood within:	<b>12 - 24 hours</b>
Remains elevated for:	Returns to normal within <b>2-3 days</b> التروبون كان يظل بالجسم تقريبا لمدة ١٠ أيام بينما هنا الـ CK-MB يقعد لمدة أقل وهي ٣-٢ أيام ، بنكتشف فائدتها بعدين
Relative index	<b>Relative index = CK-MB mass / Total CK x 100</b> More than 5 % is indicative for MI (means there are a 5% of CK-MB in the body normally) نحسب الاندكس بالمعادلة الموجودة وإذا كان الناتج أكبر من ٥% فهذا دليل على حدوث الـ MI
Advantages and disadvantages:	<b>Advantages</b>
	Useful for early diagnosis of MI
	<b>Useful for diagnosis of re-infarction</b> الأشخاص اللي يصير لهم MI نفس المرأة عندما تجهض ، إذا أجهضت مره تكون معرضة للإجهاض مره أخرى! فلنفترض إن عندنا شخص تعالج من الـ MI ، وبعد أسبوع أعندا فحوصاته علشان نتأكد إن الـ MI مارجع له مره ثانيه ، ولقينا عنده الـ CK-MB عالي!! بالرغم من انه ما يظل بالجسم الا ٣ أيام !! فهذا دليل على إن الـ MI رجع له مره ثانيه.
<b>disadvantages</b>	Not significant if measured after 2 days of MI (delayed admission) Not highly specific (elevated in skeletal muscle damage)

## 3-Myoglobin

### What is it?

- Myoglobin is an oxygen binding protein of cardiac and skeletal muscle.
- It is a sensitive marker of cardiac damage. **"an Early marker"**

Appears in:	It Appears in blood earlier than other CK-MB ( <b>within 1-4 hours</b> ) due to its low molecular weight and cytoplasmic location.
Its Specificity:	Not specific because it is elevated in:
Elevated in:	Muscle disease/injury
	Acute and chronic renal failure

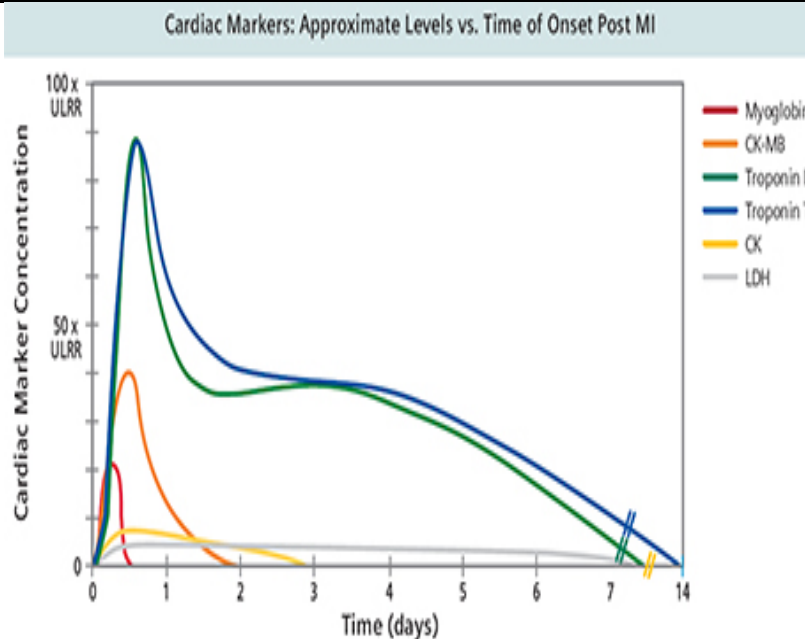
## B-type natriuretic peptide (BNP)

What is it?	BNP is a <b>peptide hormone</b> produced by <u>the ventricles of the heart</u> in response to: <b>Myocardial stretching</b> and <b>ventricular dysfunction after MI.</b>
What does it cause?	It causes <b>vasodilation, sodium and water excretion</b> and reduces blood pressure (The heart has to work harder in case of MI , because a part of it is lost, and it will fatigue due to the overwork. So this peptide will be released to relieve the heart and cause vasodilation .and reduce bp)
Used for:	<b>diagnosis of congestive heart failure (CHF)</b>
Facts:	-its serum levels are high in some <b>pulmonary diseases</b> , but in heart failure its levels are <b>markedly high</b> . -it is an important marker for differential diagnosis of <b>pulmonary diseases</b> and <b>congestive heart failure</b> .

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

What is it?	- A <b>cytosolic protein</b> involved in fatty acid transport and metabolism. - It's a <b>promising</b> marker to be used in combination with <b>troponins</b> .
Where does it exist?	Higher amounts in <b>myocardium</b> than in <b>brain, kidney</b> and <b>skeletal muscle</b>
When does it appear?	- <b>Appears in blood as early as 30 minutes</b> after acute ischemia. - <b>Peaks</b> in blood in <b>6-8 h</b> , - <b>Returns to normal levels in 24-30 h</b> .
Not a suitable marker for:	Patients presenting more than <b>6-8 h</b> . from the onset of symptoms, <b>why?</b> Due to <b>rapid renal clearance</b> of this marker.

# Time-course of plasma enzyme changes



Plasma enzymes follow a pattern of activities after MI

The initial lag phase lasts for about 3 hours

(lag phase : nothing happen in this duration)

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

(because this rapid rise & fall are not normal, so if you notice it you'll know there's a problem in the heart)

Requires presence of **at least two** of these characteristics

# Diagnosis of AMI

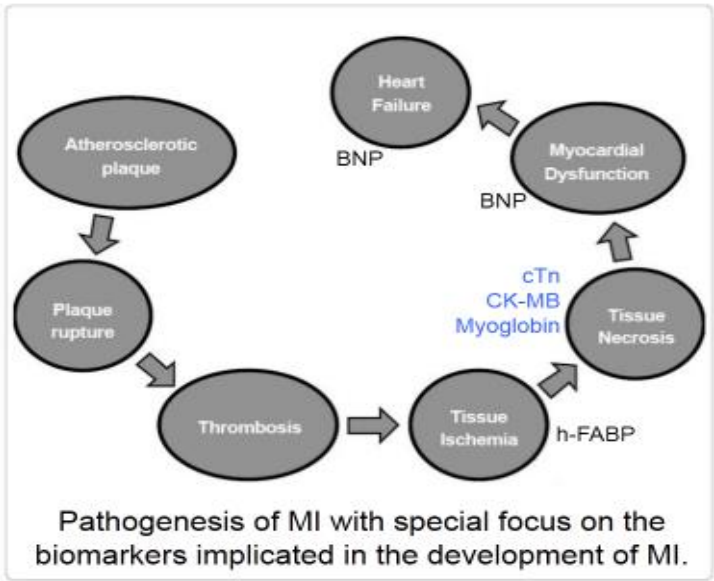
Ischemic symptoms

Typical rise and fall pattern of a cardiac marker in plasma

Typical ECG pattern(changes)

Typical rise and gradual fall of cardiac troponins

More rapid rise and fall of CK- MB



## Marker changes in blood

Enzyme / Protein	Detectable(hours)	Peak value(hours)	Duration(days)
Cardiac troponins	3-4	~48	Up to 10
CK-MB	3-10	12-24	2-3
Myoglobin	1-4	6-9	1

## Cases:

**1- 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???**

- He has an **elevated troponin** plus a **typical heart attack symptoms**.

- This is sufficient to diagnose a MI by the most recent definition, even in the absence of ECG changes.

2 out of 3 characteristics happen in this case, so he suffered a MI.

**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 <6%). Troponin was undetectable. Comment on these results.**

**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.**

(Briefly, this is NOT a MI case. Don't be confused between muscle damage cases and MI cases)



## MCQs:

1-The following isoenzyme of creatine kinase in serum is raised in myocardial infarction:

- A. CK-BB
- B. CK-MM
- C. CK-MB

2-BNP is a heart failure marker that causes:

- A. Vasoconstriction
- B. Na resorption
- C. Decrease in blood pressure

3-CK-MB appears in blood within

- A. 3-10 hours
- B. 30 minutes
- C. 1-2 hours

4-serum enzymes helpful in clinical diagnosis of myocardial infarction are the following except:

- A. Aspartate transaminase
- B. Alanine transaminase
- C. hFABP

5-Myoglobin is elevated in all of the following except :

- A. Cardiac damage
- B. Cancer
- C. Muscle injury
- D. Acute renal failure

6-At stage of tissue ischemia which biomarker is high:

- A. BNP
- B. CK-MM
- C. hFABP

7-cardiac muscle has the highest amount of :

- A. CK-BB
- B. CK-MB
- C. CK-MM

8-cTnT binds to :

- A. Tropomyosin
- B. cTnI
- C. Myoglobin

9-your diagnosis of a patient that has high troponin T levels is:

- A. Renal failure
- B. Pulmonary fibrosis
- C. Acute coronary syndrome

10-creatine kinase is found in:

- A. Myocardium
- B. Brain
- C. Muscles
- D. All of the above

1-C  
2-C  
3-A  
4-B  
5-B  
6-C  
7-B  
8-A  
9-C  
10-D