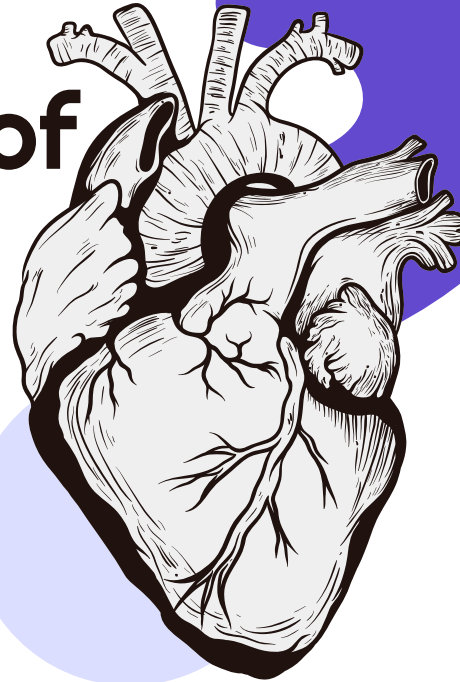# Biochemical Markers of myocardial infarction

**Editing File**

COLOR INDEX:
MAIN TEXT (BLACK )
FEMALE SLIDES ( PINK)
MALE SLIDES ( BLUE)
IMPORTANT (RED)
DR'S NOTE ( GREEN )
EXTRA INFO (GREY)

# Objective

**01**
Describe the general sequence of events of myocardial infarction (MI).

**02**
List the criteria for diagnosis of MI.

**03**
Discuss the features of an ideal MI marker.

**04**
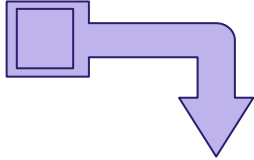Understand the significance of changes in plasma marker levels over time.

**05**
Identify the properties and diagnostic value of cardiac troponins, creatine kinase, h-FABP and BNP.
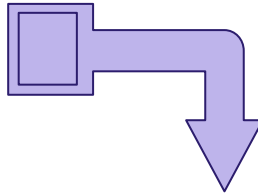
**06**
Know about markers with potential clinical use.
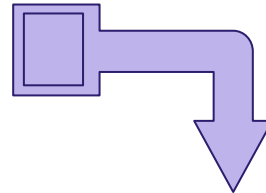
# Myocardial Infarction (MI)

Occlusion of coronary arteries

→

Restricted blood supply(O2) to heart tissue **(ischemia)**

→

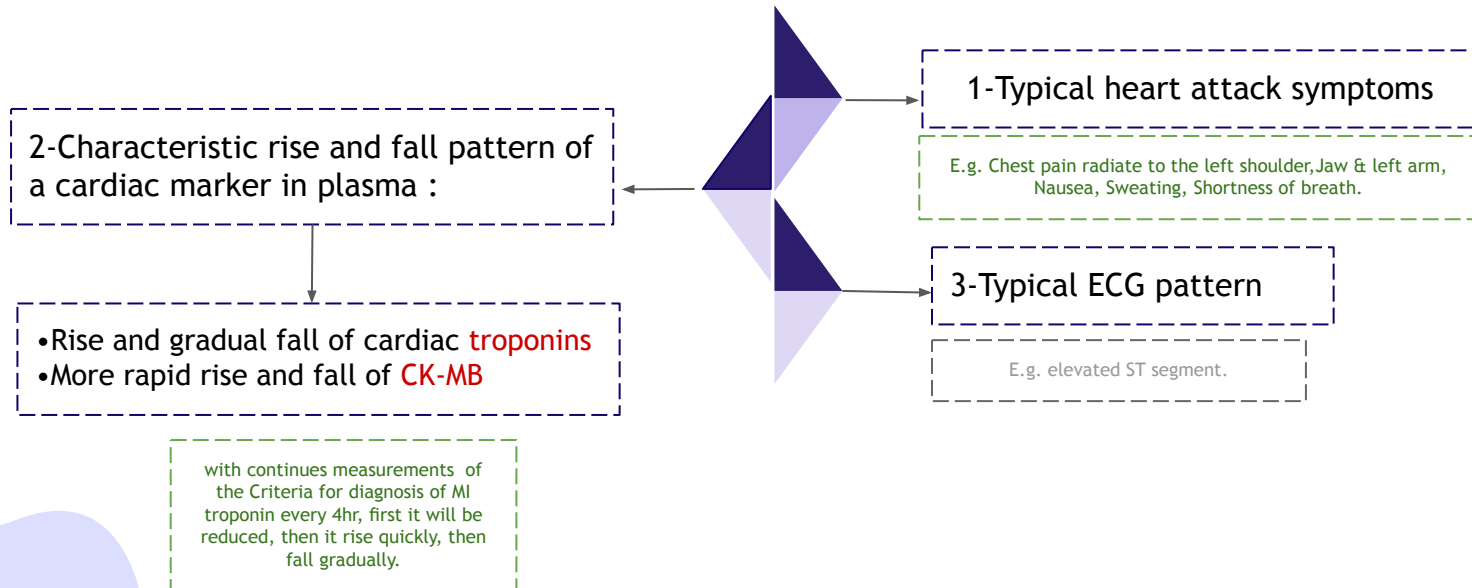Damage to heart tissue **(infraction)**

→

Release of enzymes and other proteins into the blood **(markers)**

# 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 radiate to the left shoulder,Jaw & left arm, Nausea, Sweating, Shortness of breath.

3-Typical ECG pattern

E.g. elevated ST segment.

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 CK-MB

with continues measurements of the Criteria for diagnosis of MI troponin every 4hr, first it will be reduced, then it rise quickly, then fall gradually.

# Features of an Ideal Cardiac Marker

**1-High concentration in the myocardium**

**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

**4-Rapid release into plasma following myocardial injury**

**5-Good prognostic value**
Strong correlation between plasma level and extent of myocardial injury

**6-Easily measured**
Detectable by rapid, simple and automated assay methods.

يعني كل ما كانت كمية biomarker كثيرة في الدم كل ما كان الجزء المتضرر أكبر

# Plasma Cardiac Markers

→ Cardiac markers = Cardiac enzymes

## Current MI markers

Cardiac troponin T (cTnT)

Cardiac troponin I (cTnI)

Creatine kinase-MB (CK-MB)

Myocardium Bound

## Markers with potential clinical use

Heart fatty acid binding protein (h-FABP)

For detecting heart tissue ischemia

## Markers no longer used

Aspartate Transaminase (AST)

Lactate dehydrogenase (LDH)

Ischemia modified albumin (IMA)

Myoglobin

Low specificity

# Markers of Diagnostic Value

**In myocardial infarction**

Cardiac troponin T and I

Creatine kinase (CK-MB)

**In tissue ischemia**

Heart fatty acid binding protein (h-FABP)

Useful in early stage diagnosis

**Heart failure**

B-type natriuretic peptide (BNP)

Useful in late stage diagnosis

# Time-Course of Plasma Enzyme Changes

Girls doctor said you need to know these numbers

| Time-course of plasma biochemical marker elevation after changes after MI | | | |
|---|---|---|---|
| Enzyme | Abnormal activity detectable (Hours) | Peak value of abnormality (Hours) | 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 |
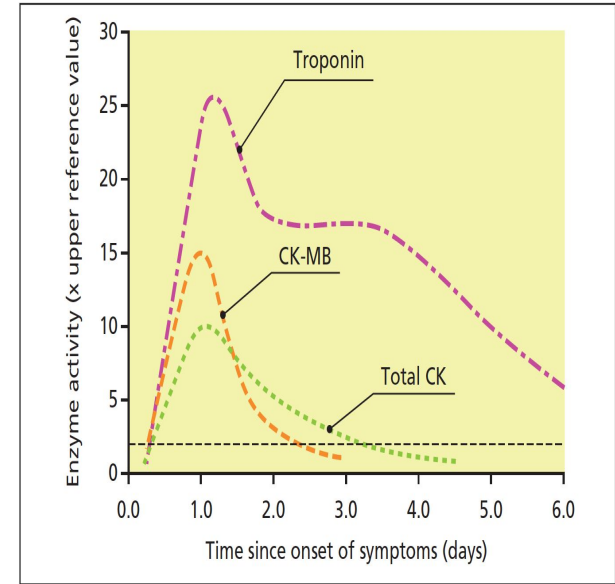
# Time-Course of Plasma Enzyme Changes

- Plasma enzymes follow a pattern of activities after MI

- The initial lag phase lasts for about 3 hours

  Lag phase: a phase in which the conc. of plasma enzymes has not changed yet.
  "No elevation in markers appears"

- 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

  *CK-MB: Rapid rise and fall. Troponin: Rapid rise and gradual fall.

**Blood samples collected after MI:**

- Baseline (upon admission)

- Between 12 and 24 hours after the onset of symptoms

# Troponins

-Troponins are structural proteins in cardiac myocytes and in skeletal muscle
-Cardiac troponins (cTn) are structurally different from muscle troponins .
-Involved in the interaction between actin and myosin for muscle contraction.
-Highly specific markers for detecting MI.

troponin C is present in both cardiac and skeletal muscle cells, while cTnI and cTnT are expressed as cardiac muscle-specific isoforms.

## Two main cardiac troponins (cTn)

cTn<u>I</u>
(<u>Inhibitory</u> protein)

cTn<u>T</u>
(binds to <u>T</u>ropomyosin)

## Location of cardiac troponins

Mainly bound to proteins

Small amount soluble in the cytosol

| Enzyme | Detectable in plasma | Level peaks in | Remain elevated |
|--------|---------------------|----------------|-----------------|
| Troponin | 4-6 h after MI | 12-24 h | up to 10 days |

# Troponins



- After MI cytosolic troponins are released rapidly into the blood (first few hours).
- Structurally bound troponins are released later for several days. That's why it stay in the blood for long time.
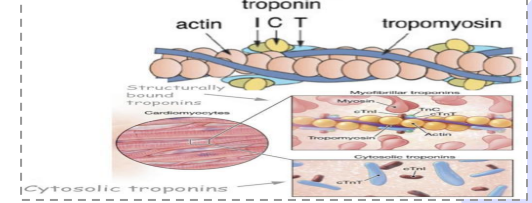
# Creatine kinase (CK)

Three main CK isoenzymes with two polypeptide chains B or M

| type | Composition | Comment |
|---|---|---|
| Skeletal Muscle | 98% CK-MM<br>2% CK-MB | Elevated in muscle disease |
| Cardiac muscle | 70-80% CK-MM<br>20-30% CK-MB | Cardiac muscle has highest amount of CK-MB |
| Brain | CK-BB | - |
| Plasma | Mainly CK-MM | - |

# CK-MB

-CK-MB is more sensitive and specific for MI than total CK.
-It rises and falls transiently (last only for a short time) after MI.
-Relative index= CK-MB mass / Total CK x 100 if it is More than 5 % is indicative for MI

## CK-MB

**Advantages**

**Disadvantages**

Useful for early diagnosis of MI

Useful for diagnosis of re-infarction

Not significant if measured after 2 days of MI (delayed admission

Not highly specific (elevated in skeletal muscle damage)

| Enzyme | Detectable in plasma | Level peaks in | Remain elevated |
|--------|----------------------|----------------|-----------------|
| CK-MB | 3-10 h after MI | 12-24 h | 1.5-3 days |

# Heart fatty acid binding protein (h-FABP)
# (Heart tissue ischemia marker)

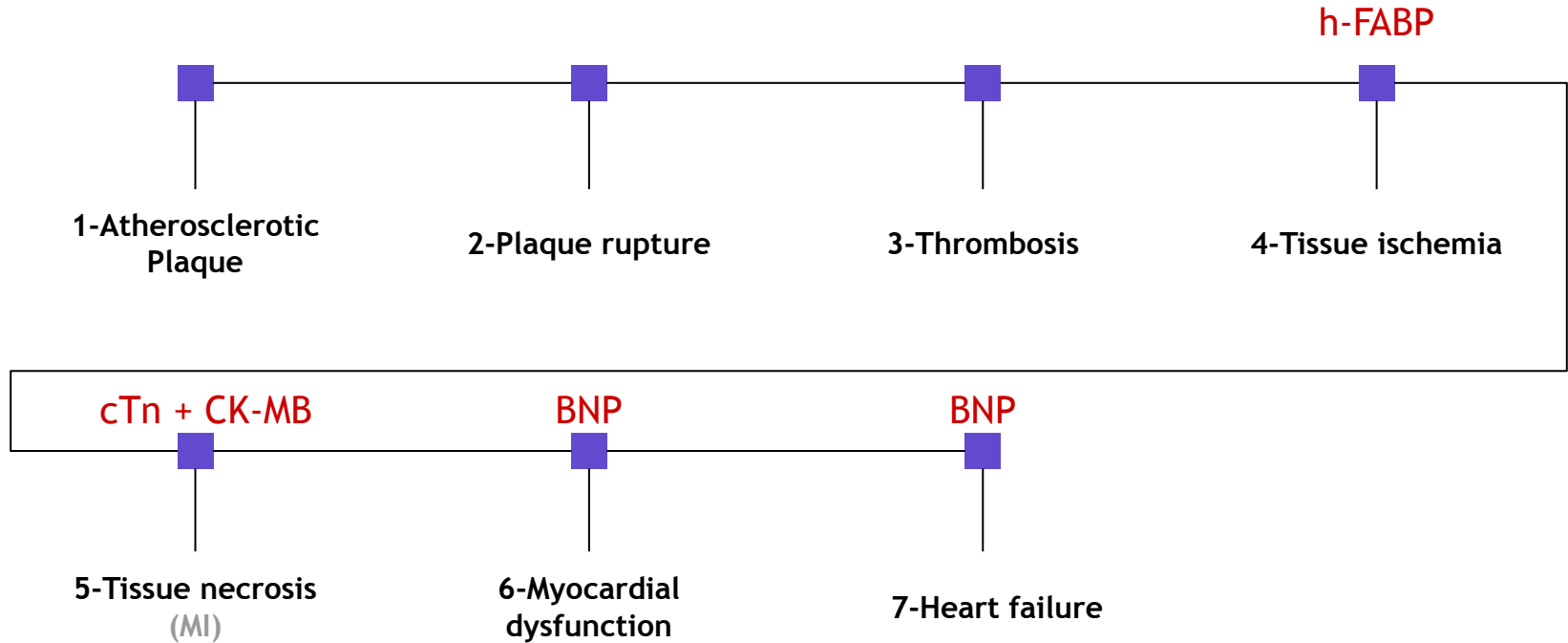| | |
|---|---|
| **Definition** | ● A cytosolic protein involved in fatty acid transport and metabolism.<br>● It's a promising marker to be used in combination with troponins. |
| **Existing** | Higher amounts in myocardium than in brain, kidney & skeletal muscle. |
| **Appearance** | ● Appears in plasma as early as 30 min. after acute ischemia.<br>● Peaks in blood in 6-8 h.<br>● Returns to normal levels in 24-30 h. |

# B-type natriuretic peptide (BNP) (Heart failure marker)

It helps in differentiation between heart disease or pulmonary disease

| | |
|---|---|
| **Definition** | A peptide produced by the ventricles of the heart in response to myocardial stretching & ventricular dysfunction after MI. |
| **It causes** | 1. Vasodilation<br>2. Sodium and water excretion<br>3. Reduces blood pressure |
| **Marker for** | Detecting congestive heart failure |
| **Facts** | ● Its serum levels are high in some pulmonary diseases but in heart failure its levels are markedly high.<br>● 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

h-FABP

1-Atherosclerotic Plaque

2-Plaque rupture

3-Thrombosis

4-Tissue ischemia

cTn + CK-MB

BNP

BNP

5-Tissue necrosis
(MI)

6-Myocardial dysfunction

7-Heart failure

# Cases

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. On admission there were no abnormalities on examination and the ECG was normal. The troponin was clearly detectable.

Comments:
Typical heart attack symptoms
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.

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 Messages

**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

# MCQ

| Q1: One of the features of an ideal cardiac marker ? | | | |
|---|---|---|---|
| A- Low sensitivity | B- Good prognostic value | C- Present in non-myocardial tissue injury | D- detectable by slow assay methods |
| Q2: A cytosolic protein involved in fatty acid transport and metabolism ? | | | |
| A- h-FABP | B- CK-MB | C-troponin | D- BNP |
| Q3: Biomarkers used to detect CHF ? | | | |
| A- CK-MB | B- BNP | C- Troponin | D- Total CK |

# MCQ

| Q1: Biomarkers used to detect ischemia ? | | | |
|---|---|---|---|
| A- BNP | B- CK-MB | C- Troponin | D-  h-FABP |
| **Q2: Biomarker is used to detect re-infarction ?** | | | |
| A- BNP | B- CK-MM | C- CK-MB | D- CK-BB |
| **Q3: A peptide produced by the ventricles of the heart in response to myocardial stretching ?** | | | |
| A- h-FABP | B- CK-MB | C- troponin | D- BNP |

# SAQ

Q1: mention the criteria for diagnosis of MI?

1. Typical heart attack symptoms 2. Characteristic rise and fall pattern of a cardiac marker in plasma 3. Typical ECG pattern

Q2:What are the main cardiac troponins and their location?

A2: slide 10

Q3:List the advantages and disadvantages for using CK-MB in diagnosing MI ?

A3: slide 12

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