# CARDIAC ISCHEMIA

GRADE: FIRST YEAR – ASHUR MEDICAL COLLEGE 2023/2024

MODULE: SYSTEMIC (CARDIOVASCULAR)/ BIOCHEMISTRY

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DATE: 8/5/ 2024

# OBJECTIVES

- Define ischemic heart disease ( IHD) coronary artery disease (CAD).
- List the cardiac biochemical markers used in confirmation the diagnosis of Myocardial Infarction.
- Identify the time of elevation and the peak of each marker after onset of chest pain.
- Choose the most appropriate biochemical marker in confirmation the diagnosis of myocardial injury and heart failure.

# COMMON ABBREVIATIONS

- Ischemic heart disease ( IHD)
- coronary artery disease (CAD)
- Right Coronary Artery (RCA):
- Right Marginal Artery (RM)
- Posterior Descending Artery (PDA)
- (posterior interventricular artery).
- Left Coronary Artery (LCA):
- left anterior descending artery (LAD)
- left circumflex artery (LCx).

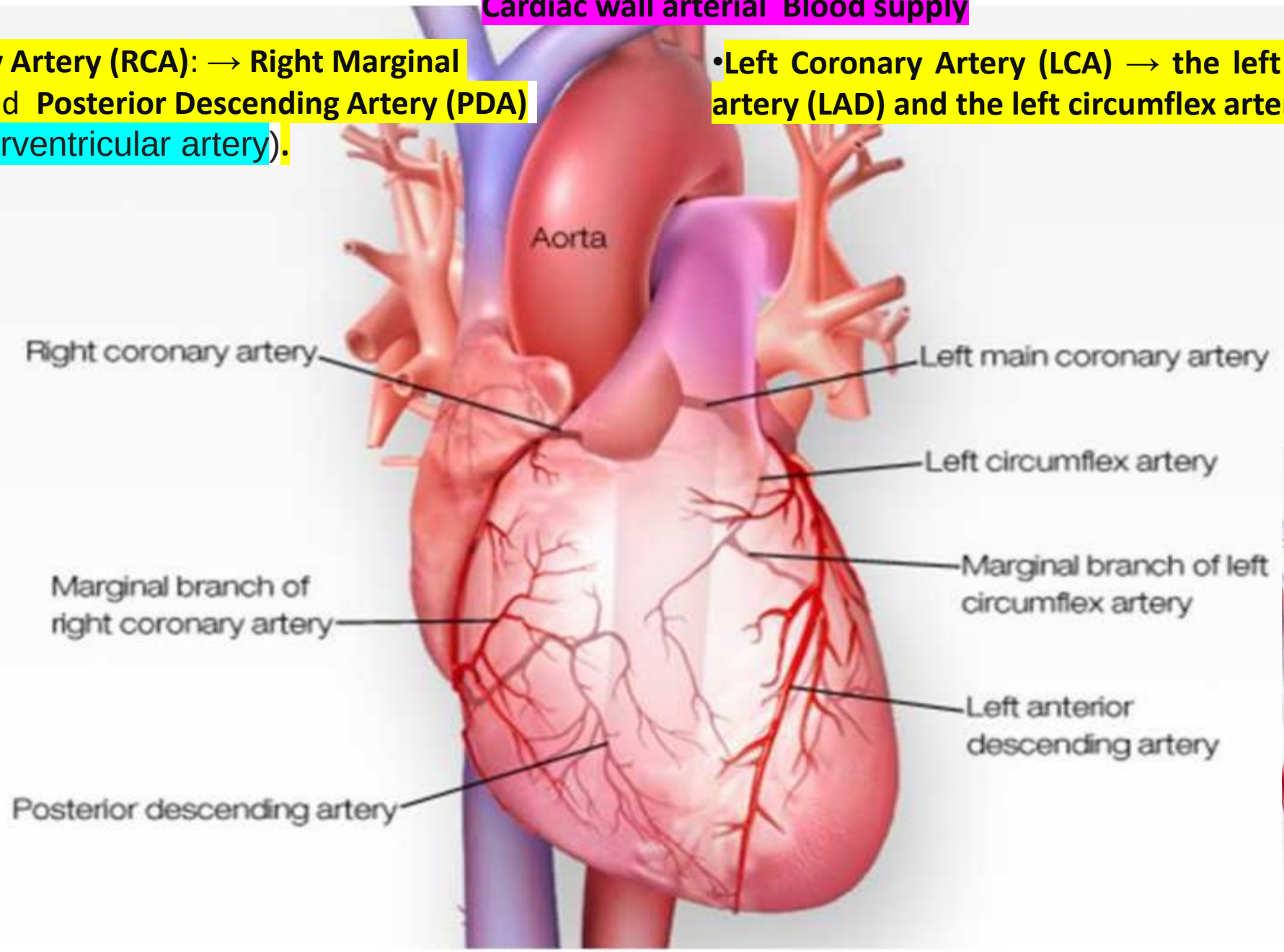
Troponin C (TnC), troponin I (TnI), and troponin T (TnT)
AST : Aspartate Aminotransferase = glutamic-oxaloacetic transaminase (SGOT :
Creatine kinase : (CK), also known as creatine phosphokinase (CPK)
CK-MB for cardiac muscle .
LDH: Lactate Dehydrogenase
BNP : Brain natriuretic peptide and NT-proBNP :N-Terminal pro-Brain Natriuretic Peptide
HDL : (high density lipoprotein)
LDL : Low density lipoprotein

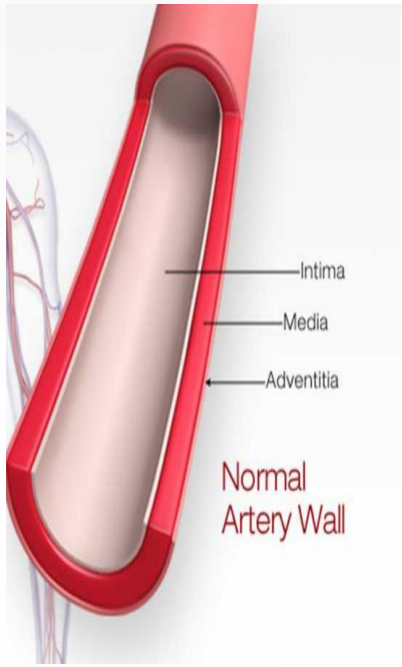
- Acute coronary syndrome (ACS) : ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI).

# Cardiac wall arterial Blood supply

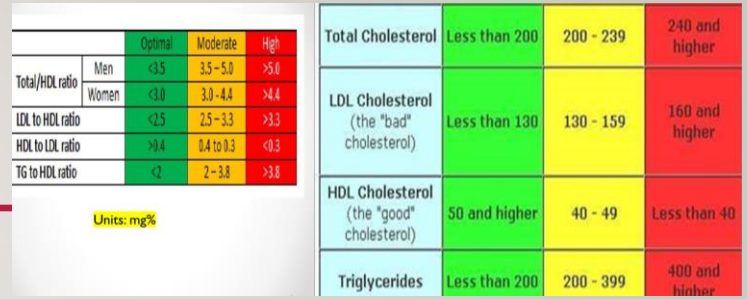
**Right Coronary Artery (RCA)**: → **Right Marginal Artery (RM)** and **Posterior Descending Artery (PDA)** (posterior interventricular artery).

•**Left Coronary Artery (LCA) → the left anterior descending artery (LAD) and the left circumflex artery (LCx).**



**Ischemic heart disease (IHD)or coronary artery disease (CAD), is a condition characterized by reduced blood flow to the myocardium due to the narrowing or blockage of the coronary arteries.**



| | | Optimal | Moderate | High |
|---|---|---|---|---|
| Total/HDL ratio | Men | <3.5 | 3.5 - 5.0 | >5.0 |
| | Women | <3.0 | 3.0 - 4.4 | >4.4 |
| LDL to HDL ratio | | <2.5 | 2.5 - 3.3 | >3.3 |
| HDL to LDL ratio | | >0.4 | 0.4 to 0.3 | <0.3 |
| TG to HDL ratio | | <2 | 2 - 3.8 | >3.8 |

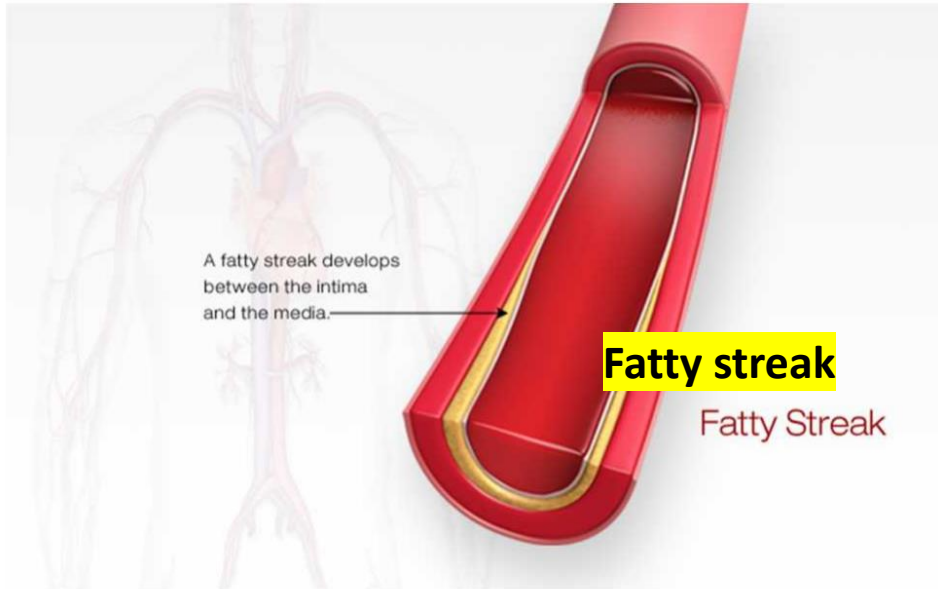
Units: mg%

| | | | |
|---|---|---|---|
| Total Cholesterol | Less than 200 | 200 - 239 | 240 and higher |
| LDL Cholesterol (the "bad" cholesterol) | Less than 130 | 130 - 159 | 160 and higher |
| HDL Cholesterol (the "good" cholesterol) | 50 and higher | 40 - 49 | Less than 40 |
| Triglycerides | Less than 200 | 200 - 399 | 400 and higher |

## Pathogenesis of Atherosclerosis

- **1-Damage to the endothelium: contributed factors blood pressure, high cholesterol levels, smoking, diabetes. Once damaged, the endothelium becomes permeable to lipids (such as low-density lipoprotein or LDL cholesterol).**
- **2- Modified low-density lipoprotein (LDL) induces the formation of foam cells (cellular lipidosis or cellular lipid retention).**
- **3- Newly formed foam cells accumulate in the arterial intima and initiate the formation of atherosclerotic lesions within the arterial wall, which at the early stages are called fatty streaks.**
- **4- Over time, the accumulated lipids, along with inflammatory cells, cellular debris, calcium deposits, and fibrous tissue, form a fibrous plaque ( atheroma) along the inner walls of the arteries, reducing blood flow.**
- **5- As plaques grow, they can narrow the arterial lumen, reducing blood flow to tissues and organs supplied by the affected arteries.**
- **6- Some plaques may become unstable and prone to rupture, leading to blood clot formation (thrombosis).**

**Fatty streaks could start at 15 year of age**

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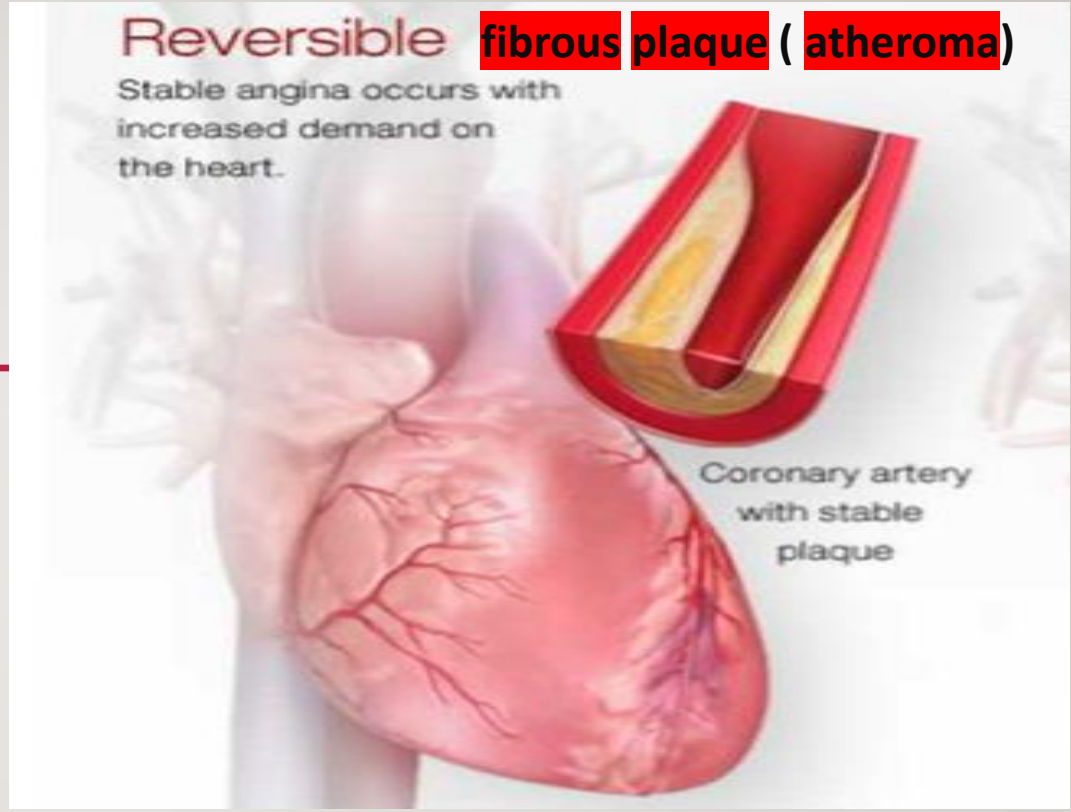
Stable angina follows a pattern and occurs during physical exertion, while unstable angina doesn't follow a pattern and can occur without physical exertion.

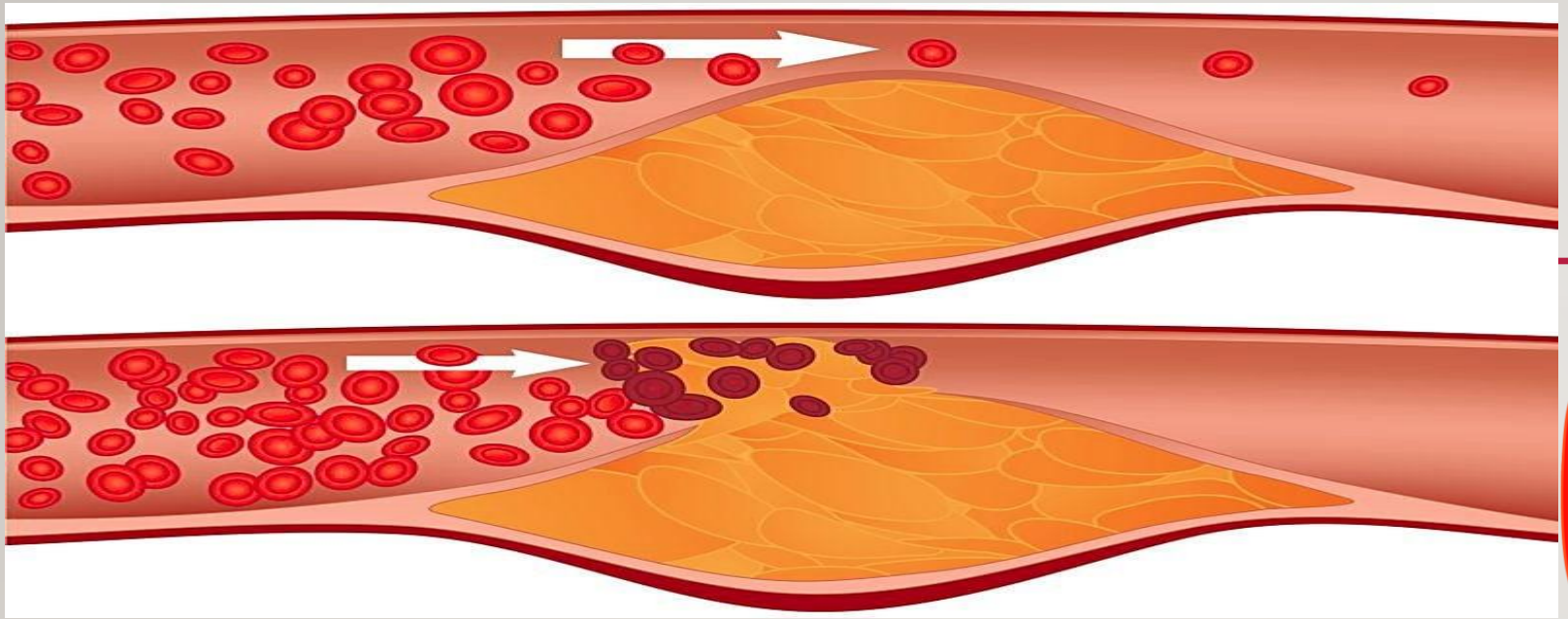


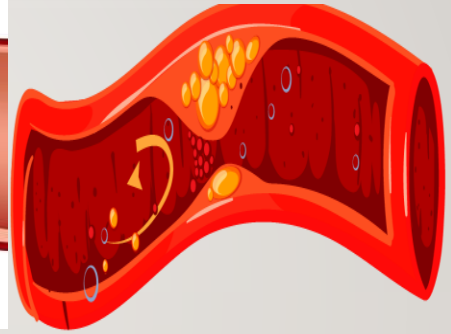

**In stable angina, the chest pain or discomfort experienced is due to temporary heart muscle ischemia, usually during physical exertion or emotional stress.**

- Unstable angina is more dangerous:&there is no ST-segment change and there is no sufficient myocardial damage to release a biochemical marker such as the troponins or CK-MB.
- Troponin I and troponin T may show slight elevations, but other cardiac biomarkers are less likely to be increased

# ACUTYE MYOCARDIAL INFARCTION

The **fibrous plaque** ( **atheroma**) may protrude into the arterial lumen, narrowing the vessel and obstructing blood flow.

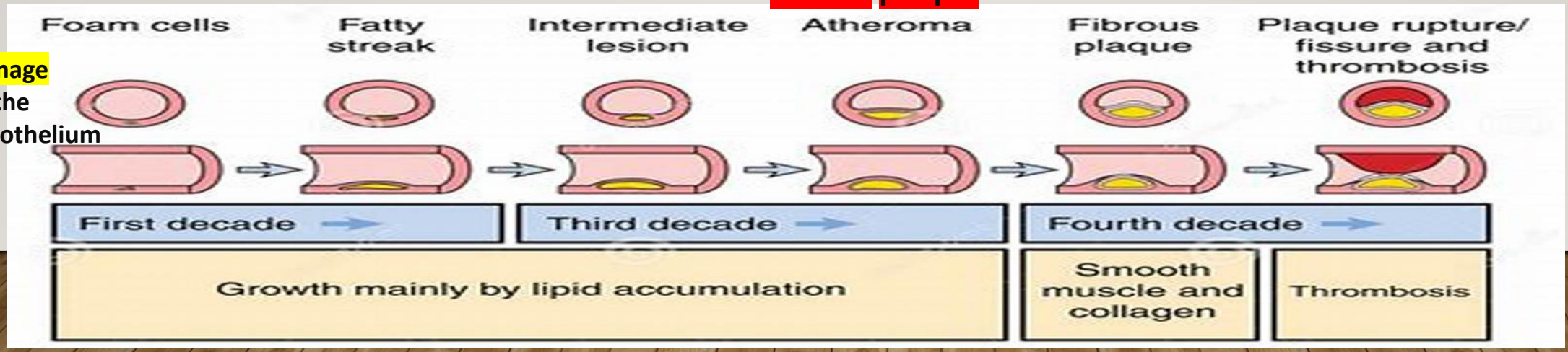




blood flow is blocked

**Rupture**, leading to the formation of blood clot. (thrombosis)

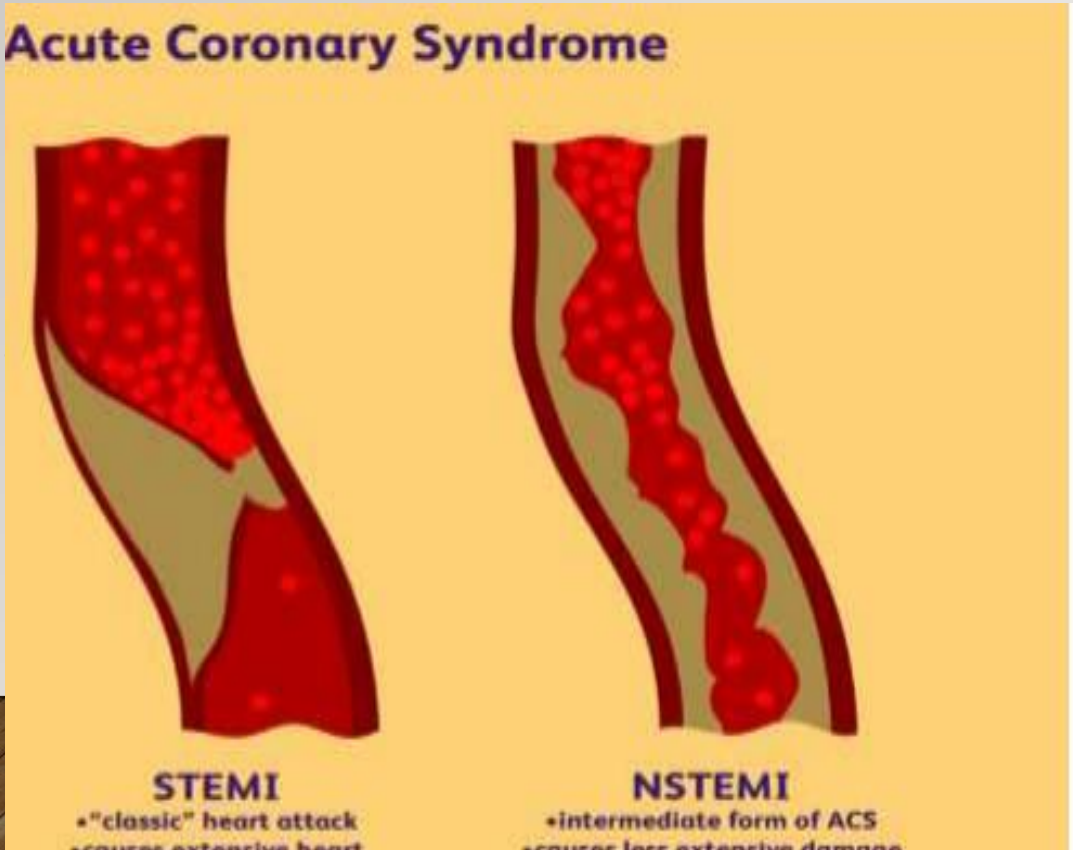
**fibrous plaque**

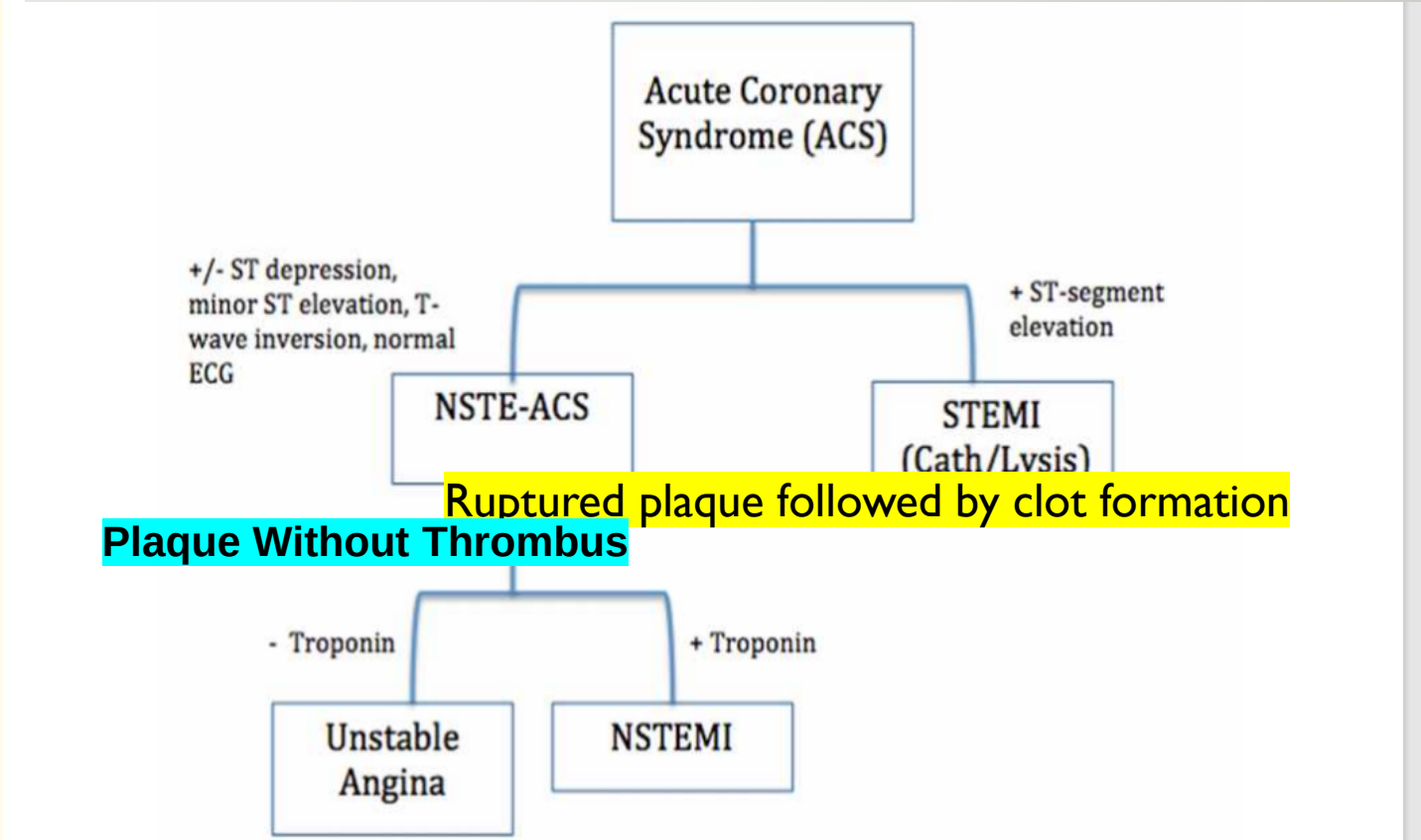



**Damage to the endothelium**

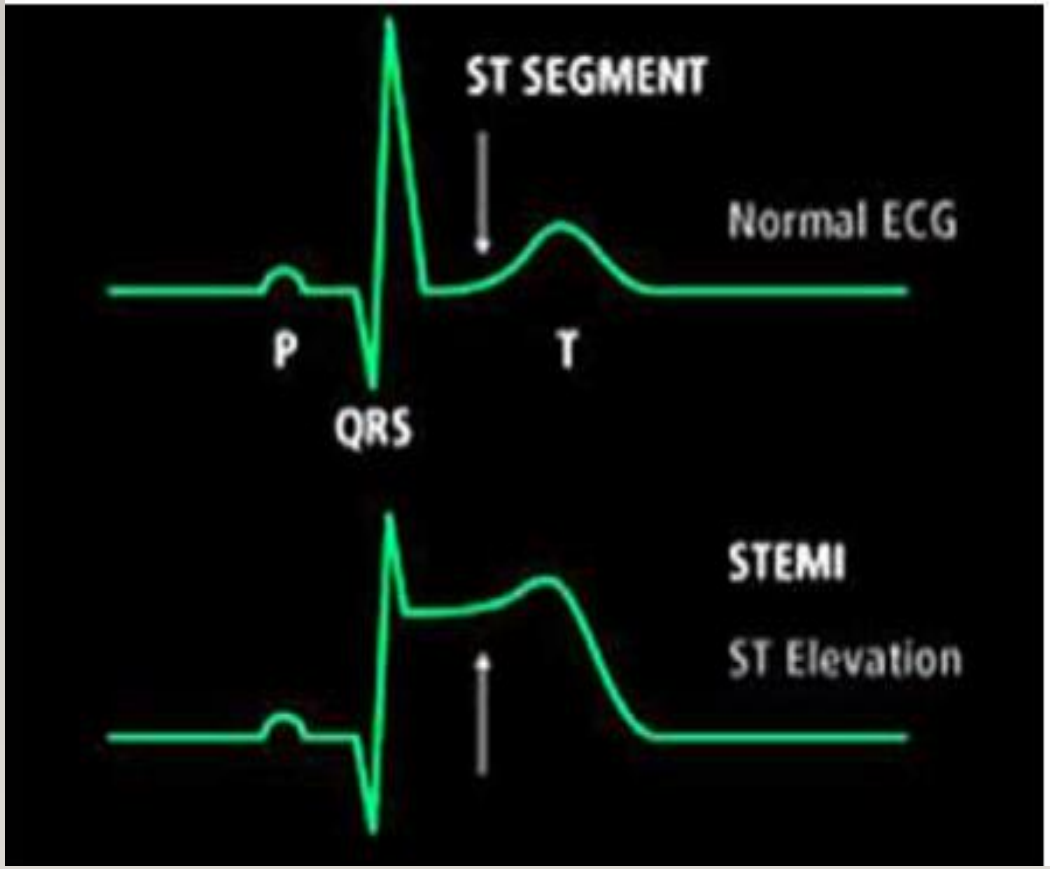
It is well known that STEMI is often associated with total coronary occlusion while NSTEMI is associated with approximately 95% of occlusion.

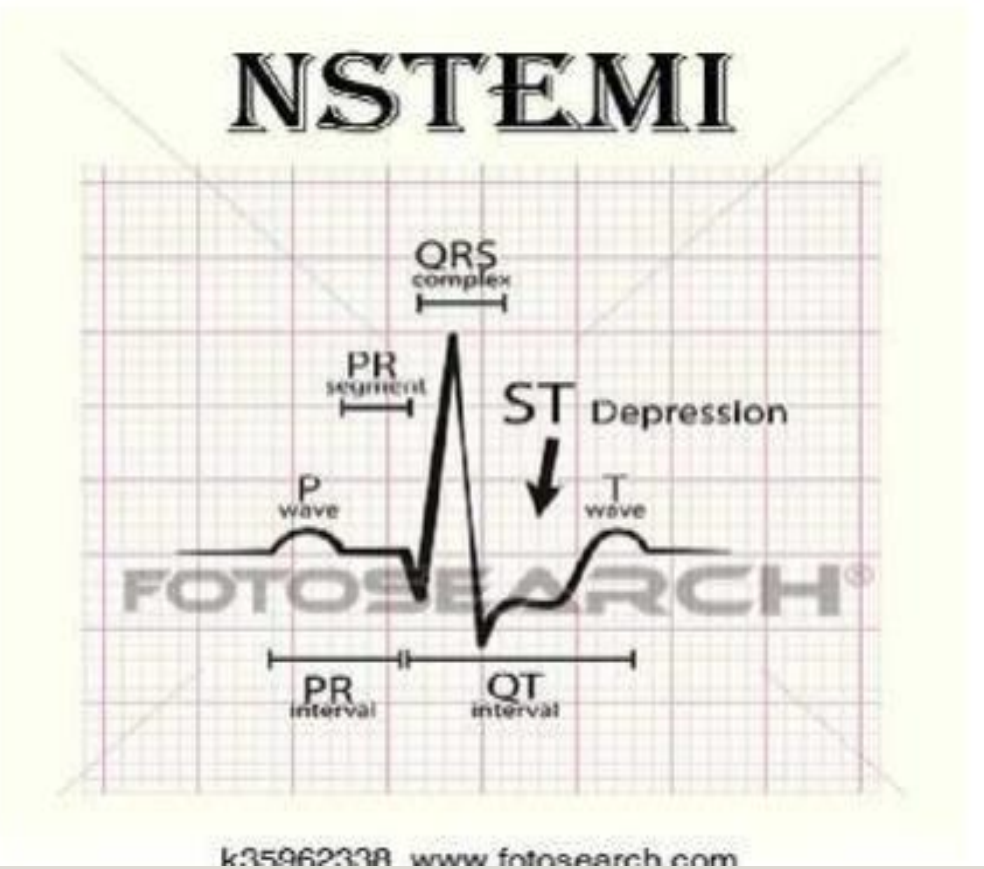
- Acute coronary syndrome (ACS) can be divided into ST-segment elevation myocardial infarction (STEMI), non-ST-segment elevation myocardial infarction (NSTEMI), and unstable angina.



- Non-ST-segment Elevation Myocardial Infarction (NSTEMI): there is no ST-segment change but there is myocardial necrosis for release of a biomarker mainly the troponins. ST-segment Elevation Myocardial Infarction (STEMI): there is ST-segment elevation and myocardial necrosis with release of a biomarker such as the troponins or CK-MB


ST SEGMENT
Normal ECG
P
T
QRS
STEMI
ST Elevation


NSTEMI
QRS complex
PR segment
ST Depression
P wave
T wave
PR interval
QT interval
FOTOSEARCH

# CARDIAC BIOCHEMICAL MARKERS

- Are substances released into the bloodstream in response to heart damage .
- They are often used in clinical practice to diagnose and monitor various cardiac conditions, e.g. :
- Ischemic heart disease.
- heart failure.
- Commonly used cardiac biomarkers:
- 1-Creatine Kinase-MB (CK-MB).
- 2- Troponins.
- 3- Myoglobin.
- 4- Brain Natriuretic Peptide (BNP) and N-terminal pro-B-type natriuretic peptide (NT-proBNP).
- 5- Lactate Dehydrogenase (LDH).
- 6- SGOT

# 1-CREATINE KINASE-MB (CK-MB)

- **1.2.2. CK-MB**
- **CK-MB for less than 5 % of total CK.**
- **CK-MB distribution 90% in CM&10% in SM .**

## CK-MB

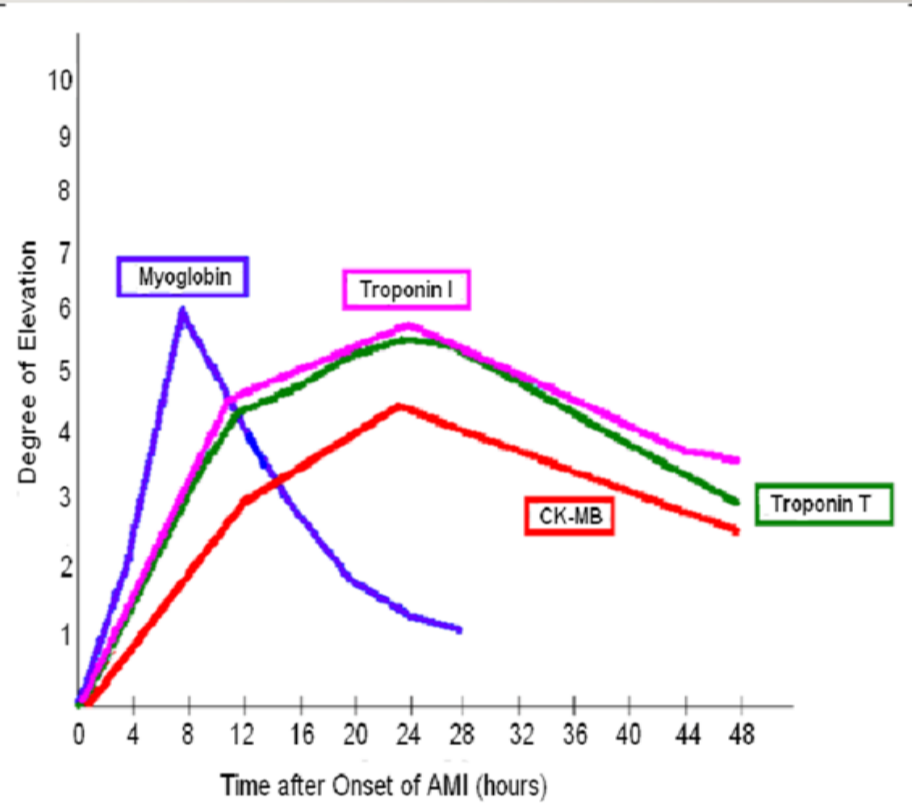
Causes of elevated CK-MB: acute myocardial infarction, myocarditis, cardiac trauma, cardiac surgery, and endomyocardial biopsy. Skeletal muscle injury can sometimes cause elevated CK-MB levels.

Total CK is less sensitive than CK-MB.

It released in blood from injured CM after 4-6 hr. of onset chest pain (MI), peak 12-24 hr., and returned to normal 48-72 hr. after chest pain.

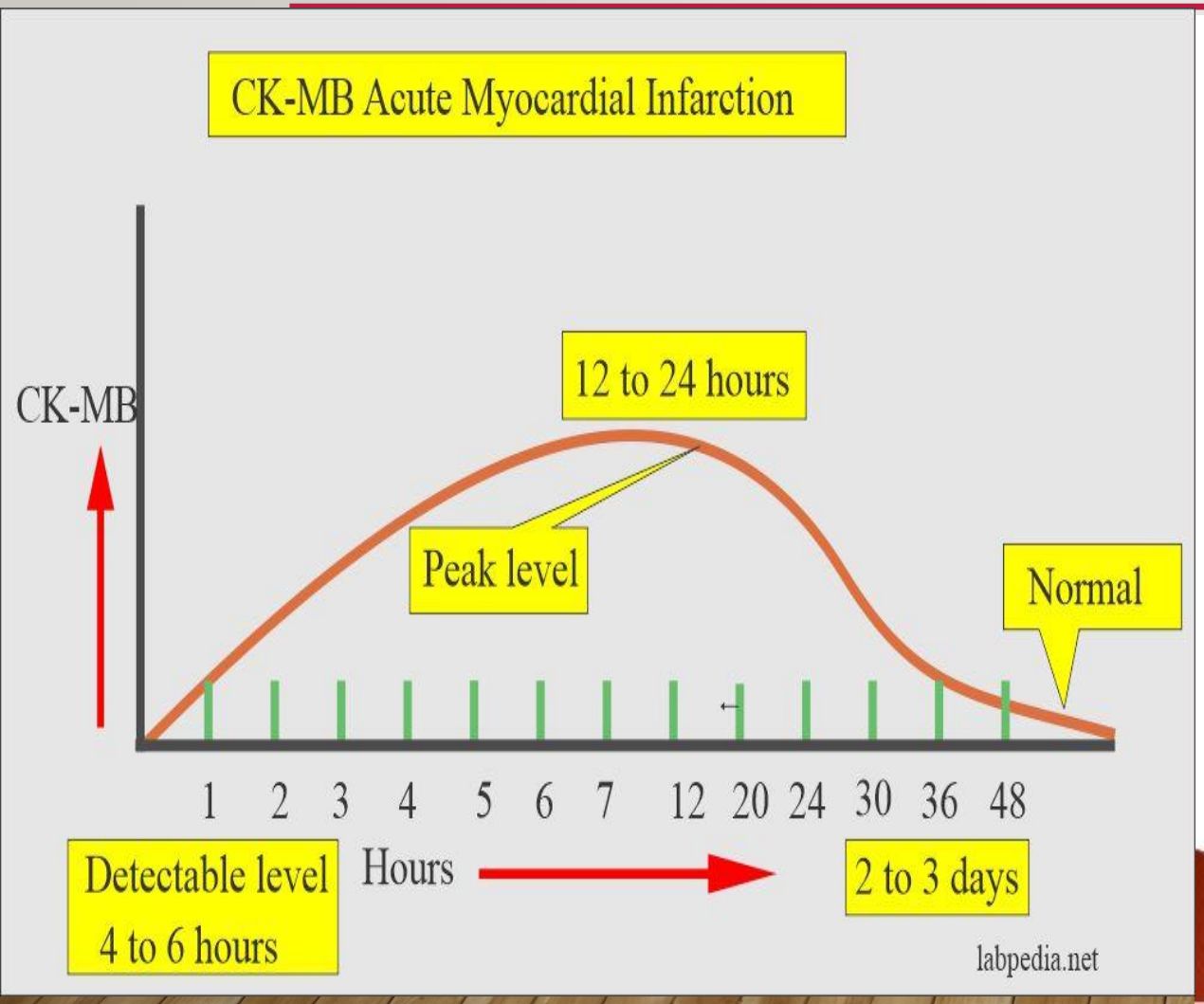
CK-MB is also useful for assessment of reinfarction or extensive of an MI because it begins to fall after 48 hr., so subsequent elevations are indicative of another event of MI.

| Marker | Detection onset (post MI) (hrs.) | range | Peak (post MI) (hrs.) | Return to Normal | Sensitivity (%) | Specificity (%) |
|---|---|---|---|---|---|---|
| CPK-MB | 4-6 | <6U/L | 12-24 | 48 – 72 (hrs.) | 50-70% | 85-90% |
| CK-MB ratio | | <3 | | | | |
| Troponin I | 2-4 | <0.08 ug/L | 12 to 24 | 5 -10 days | 90-95 | 90-95 |
| Troponin T | | | | 5-14 days | | |
| Myoglobulin | 1 - 3 | 15-120 <0.08 ug/L | 6 to 12 | 24 (hrs.) | 70-90 | 40-60 |
| LDH | 12 - 24 | 40 - 280 (IU/L) | 48 - 72 | longest Days - weeks | 40-60 | 60-70 |
| SGOT (AST) | 4-6 | | 24-48 | 5 - 7 days | High | low |
| | | | | | AST/ALT ratio of 0.63 high sensitivity and specificity | |



# CK-MB RATIO

The ratio of CK-MB (creatine kinase-myocardium) to total CK (typically CK-MM + CK-MB), expressed in %.




$$\text{Relative Index} = \frac{\text{CK-MB}}{\text{Total CK}} \times 100$$

*The relative index allows the distinction between increased total CK due to myocardial damage and that due to skeletal or neural damage.

*A relative index exceeding 3 is indicative of AMI

# 2- TROPONINS

**Introduction**

- Troponins are a group of proteins found in skeletal and cardiac muscle fibers. They play a crucial role in both cardiac and skeletal muscle contraction by regulating the interaction between actin and myosin, which is necessary for muscle contraction to occur.
- There are three main subunits of troponin: troponin C (TnC), troponin I (TnI), and troponin T (TnT).
- 2.1. Troponin C (TnC).
- 2.2. Troponin I (TnI)
- 2.3. Troponin T (TnT)

# 2.1. TROPONIN C (TNC).

- This subunit binds to calcium ions, which is essential for initiating muscle contraction. When calcium ions bind to troponin C, it triggers a conformational change in the troponin complex, releasing Troponin I inhibitory effect on the interaction between actin and myosin (Troponin I no further inhibitory ). In brief Troponin C initiates muscle contraction indirectly by promoting the interaction between actin and myosin.

Troponin C (TnC) is found in both cardiac and skeletal muscles and is not typically used as a biomarker for cardiac injury.
On the other hand
Troponin T (TnT) and troponin I (TnI) are specific to cardiac muscle.

# TROPONIN I (TNI)

- Troponin I inhibits the interaction between actin and myosin in the absence of calcium ions when the muscle is at rest. When calcium ions bind to troponin C, troponin I undergoes a conformational change, releasing its inhibitory effect on actin and allowing for muscle contraction to occur.

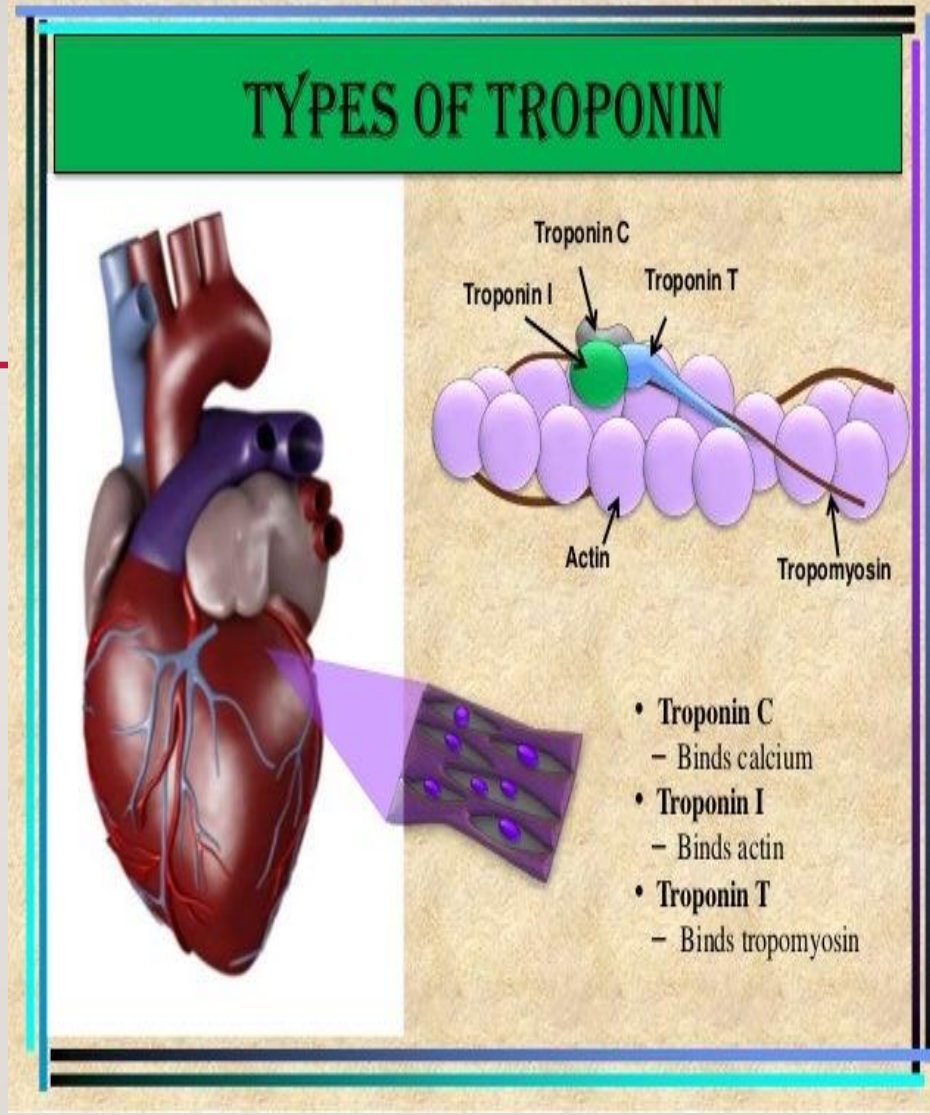
# TROPONIN T (TNT):

- Troponin T anchors the troponin complex

to the tropomyosin molecule and helps in positioning troponin

on the actin filament.

The cardiac subtype of troponin T is especially useful in the laboratory diagnosis of heart attack because it is released into the blood-stream when damage to heart muscle occurs.



# TROPONINS TEST

Troponin I and troponin T tests are commonly used for diagnosing and monitoring acute coronary syndromes

Troponin I and T are the most sensitive and specific tests for myocardial damage (MI). Because they have high sensitivity & specificity compared with CK-MB, .

They are also measured in the blood to differentiate between unstable (negative ) and myocardial infarction [positive result]- in patients with chest pain.

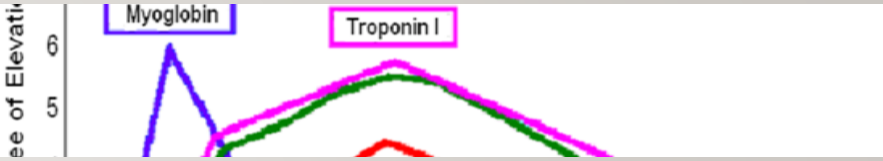
[Tn I and TnT] help to exclude elevations of CK with skeletal muscle trauma (negative troponin +positive CK-MB)






# Troponin

| | | | | | | |
|---|---|---|---|---|---|---|
| Troponin I | 2-4 | <0.08 ug/L | 12 to 24 | 5 -10 days | 90-95 | 90-95 |
| Troponin T | | | | 5-14 days | | |




Pattern of elevation: After cardiac myocyte injury (MI), troponin is released in 2-4 hr., peak 12-24 hr. and persists for up to 5-10 days for I and 2 weeks for T.

**Patients with suspected NSTEMI should have a troponin measured at presentation. If negative on presentation it should be repeated 6 to 9 hours later [after chest pain].**

| Marker | Detection onset (post MI) (hrs.) | range | Peak (post MI) (hrs.) | Return to Normal | Sensitivity (%) | Specificity (%) |
|---|---|---|---|---|---|---|
| CPK-MB | 4-6 | <6U/L | 12-24 | 48 – 72 (hrs.) | 50-70% | 85-90% |
| CK-MB ratio | | <3 | | | | |
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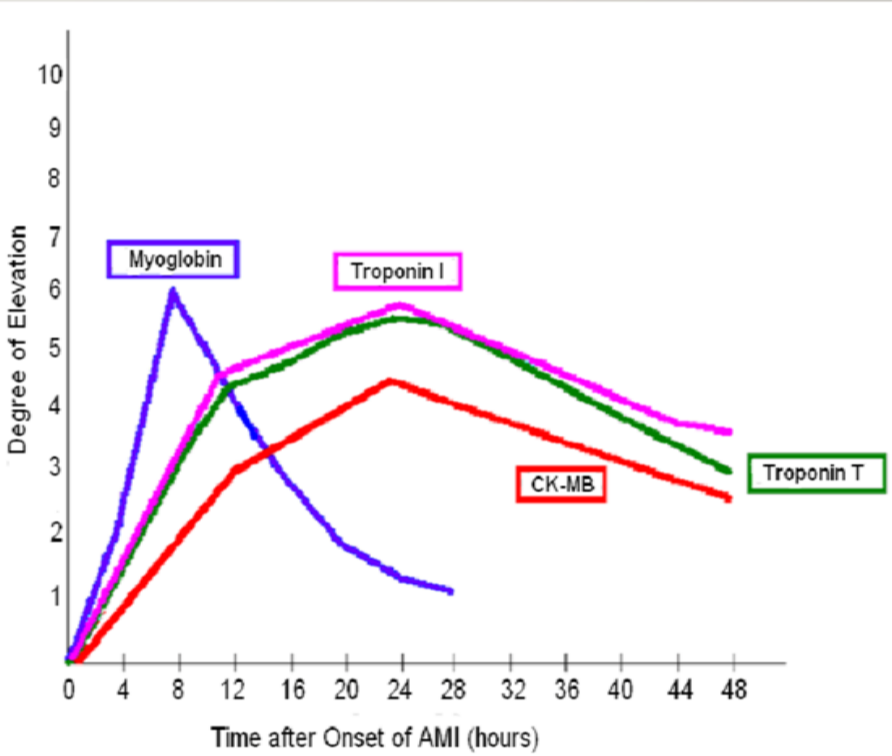
| Myoglobulin | 1 - 3 | 15-120 <0.08 ug/L | 6 to 12 | 24 (hrs.) | 70-90 | 40-60 |
| LDH | 12 - 24 | 40 - 280 (IU/L) | 48 - 72 | longest Days - weeks | 40-60 | 60-70 |
| SGOT (AST) | 4-6 | | 24-48 | 5 - 7 days | High<br>AST/ALT ratio of 0.63 high sensitivity and specificity | low |



# TROPONIN TEST POSITIVE RESULTS MAY BE SEEN IN :

1. Renal (kidney) failure
2. Chronic heart failure
3. Sepsis (severe blood infection)
4. Pulmonary embolism
5. Myocarditis
6. Aortic dissection
7. Cardiotoxic chemotherapy
8. Blunt chest trauma
9. Strenuous exercise (such as endurance athletes)

# 3. MYOGLOBIN

| | | | | | | |
|---|---|---|---|---|---|---|
| Myoglobulin | 1 - 3 | 15-120 <0.08 ug/L | 6 to 12 | 24 (hrs.) | 70-90 | 40-60 |




- It has the advantage of responding very rapidly, rising within 2 hr. after MI and falling earlier(24 hrs) than CK-MB or troponin. Increased in Heart attack , Skeletal muscle trauma, (rhabdomyolysis), myositis .

| Marker | Detection onset (post MI) (hrs.) | range | Peak (post MI) (hrs.) | Return to Normal | Sensitivity (%) | Specificity (%) |
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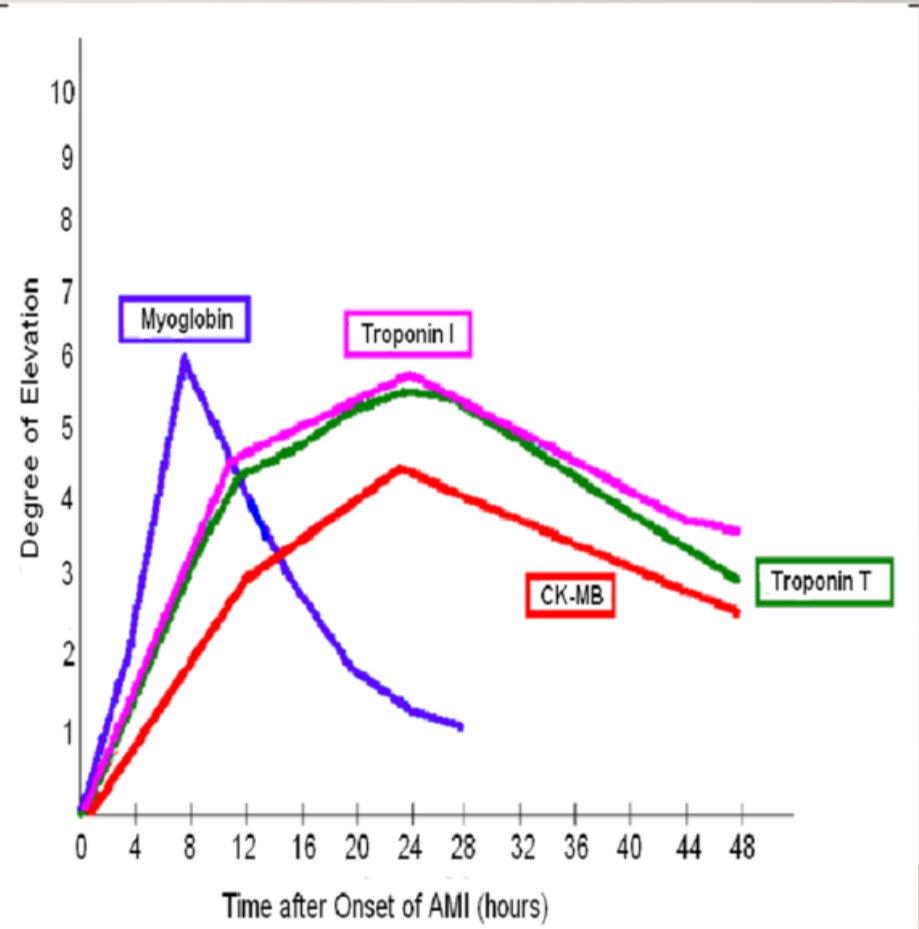

# 4- LDH

**LDH levels are often monitored in conditions such as myocardial infarction (heart attack), liver disease, muscle disorders, hemolytic anemia, and certain cancers.**

| | | | | | | |
|---|---|---|---|---|---|---|
| LDH | 12 - 24 | 40 - 280 (IU/L) | 48 - 72 | longest Days - weeks | 40-60 | 60-70 |




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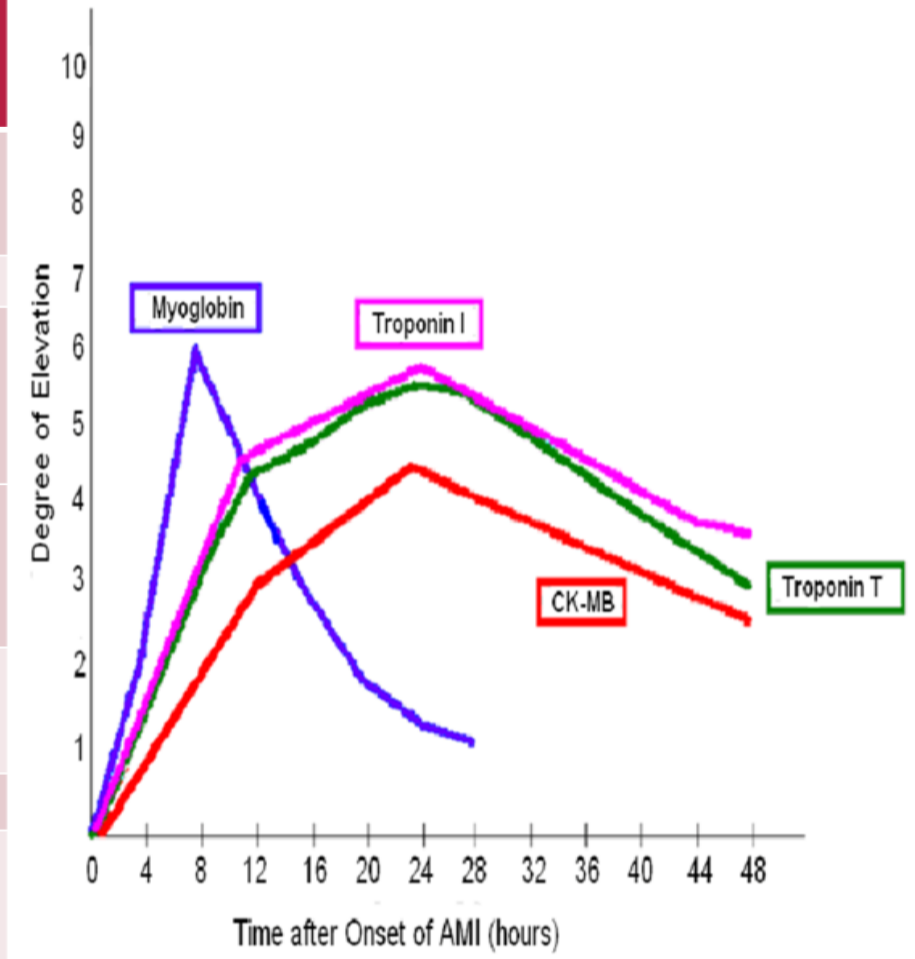
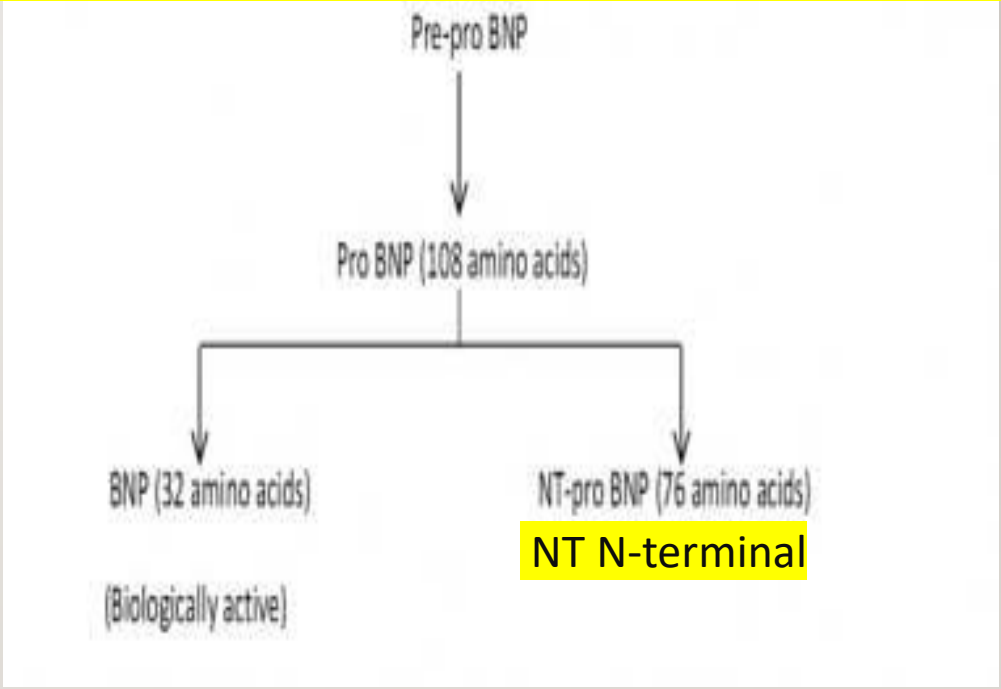


# 5.BRAIN NATRIURETIC PEPTIDE (BNP)

- BNP is synthesized as a prohormone called pro-BNP



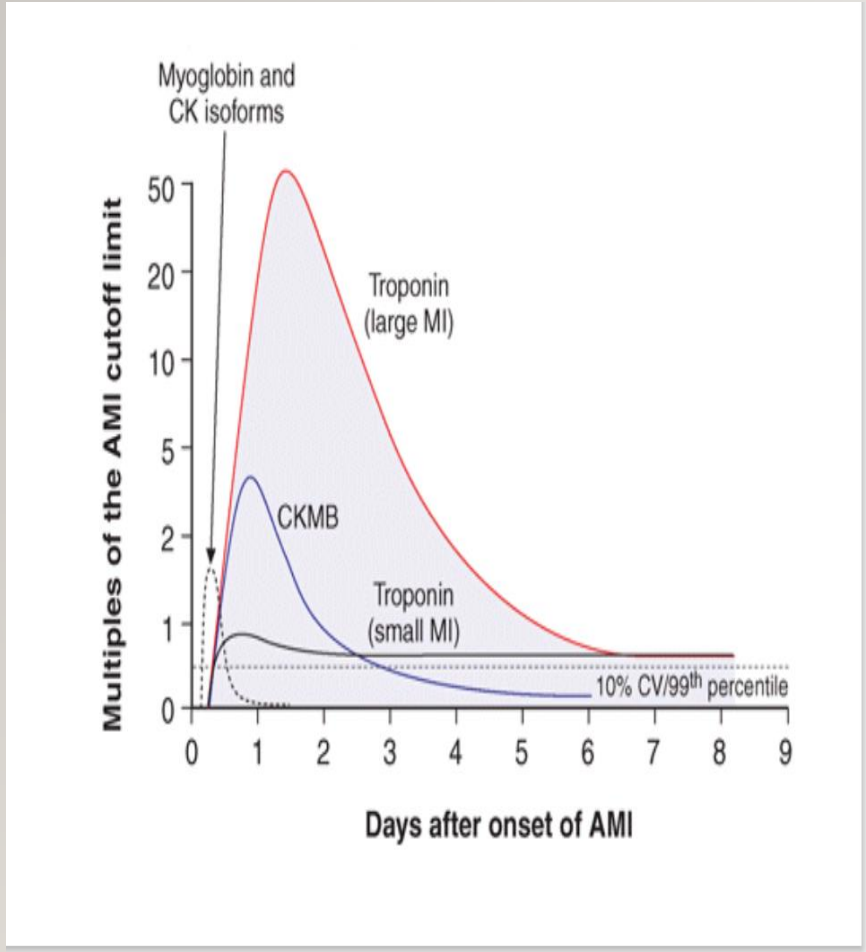

PreproBNP, which is produced by the heart ventricles

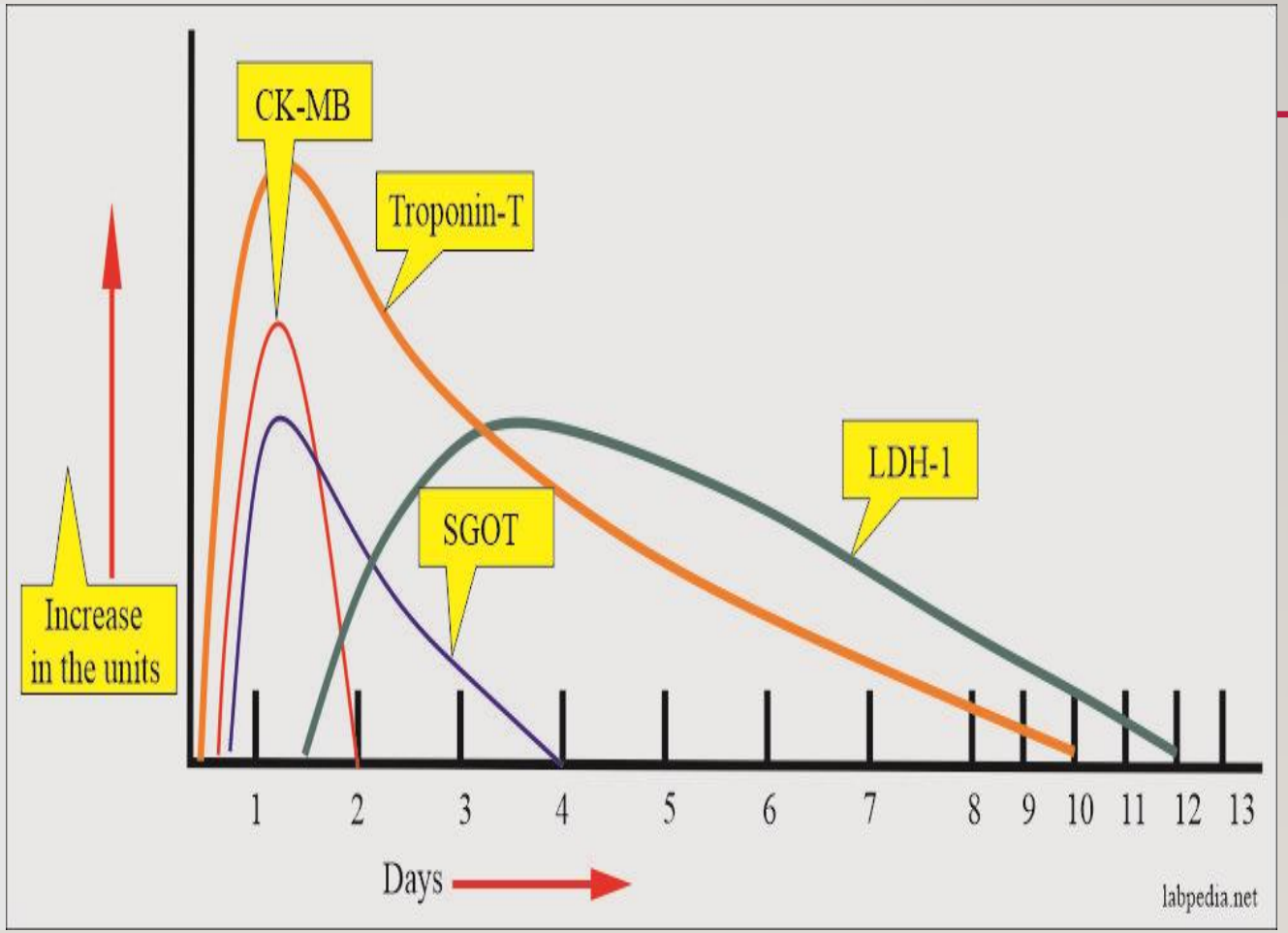



Increased in patients with heart failure [HF].

BNP plays a crucial role in regulating blood pressure and fluid balance in the body. It acts as a vasodilator, promoting the excretion of sodium and water by the kidneys.

# RETURN TO NORMAL IN DAYS : TROPONINS AND LDH



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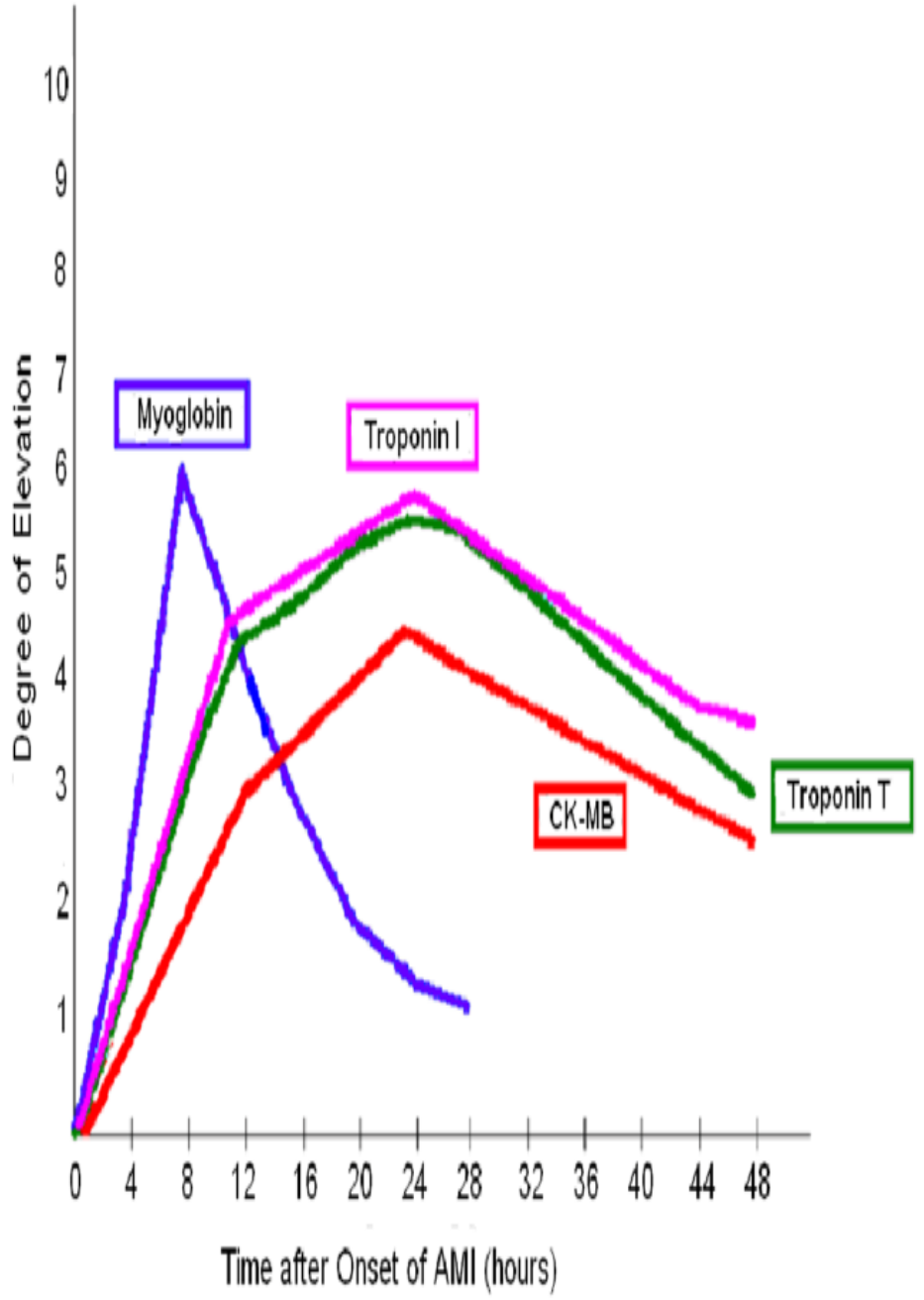

# SUMMARY

- 1. Troponin I and T are the most sensitive and specific tests for myocardial damage (MI). Because they have high sensitivity & specificity compared with CK-MB .
- 2. Troponins will remain elevated longer than CK-MB and myoglobulin.
- 3. Myoglobulin less sensitive but has the advantage of responding very rapidly, rising within 2 hr. after MI and falling earlier than CK-MB or troponin.
- 5. Serum BNP and NT-proBNP are the best biomarkers for heart failure assessment


Thank You

**Example: Acute chest pain of 1-hour duration, Increased Myoglobulin level, Normal ECG, and normal Troponin levels at 4, 6, and 12 hours.**
**Answer: This favors skeletal muscle rather than a cardiac cause.**

# HOMEWORK EXERCISE

- **A patient with Myocardial infarction has:**
- **An elevated Troponin I , elevated Troponin T, and elevated LDH. Both Myoglobulin level and CPK-MB level, are normal.**
- **What is the suggested time of onset for this infarction?**