University of Basrah
AL-Zahraa College of Medicine

Ministry of higher Education
and Scientific Research

CardioRespiratory Care Block

Lecture title : **Biochemical Markers of Myocardial Damage**

Date:30/1/2022

Dr. Zainab M. Mohammed

CRC Block Staff:

Dr Firas Rashid Sayil (block leader)
Dr. Ahmed Bader
Dr Nawal Mustafa
Dr Zainab Almnaseer
Dr Farqad Alhamdani
Dr Ban M. Saleh
Dr Amani Namaa
Dr. Mohammed Adil
Dr Assad Hassan
Dr Ahmed Qassim
Dr Safa Asaad
Dr Mustafa Ghazi
Dr Ilham Mohammed
Dr Zainab Muzahim

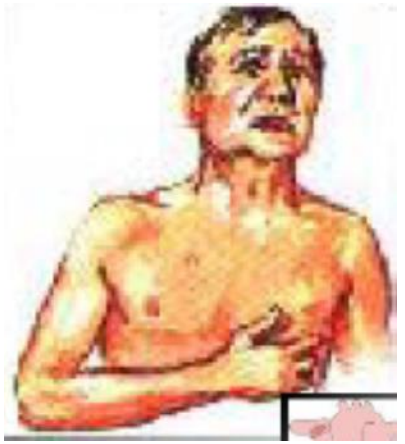
References as in the workbook and classroom.

For more detailed instruction, any question, cases need help please contact block leader at the CRC Google classroom or email.

Why cardiac markers are essential?

Chest pain is one of the most frequent reasons for visit to ER.

Chest pain of acute coronary syndrome must be distinguished from aortic dissection and pulmonary embolism which are also life-threatening.



Why cardiac markers are essential?

About 25% of patients with infarction do not experience characteristic chest pain.

Non-diagnostic ECG is found in about 50% of patients with chest pain and MI.

- **A task force drawn from a number of experts has published a consensus 'Universal Definition of Myocardial Infarction'**

  Placing biomarkers central to the definition

Myocardial infarction can be defined as

➢ rise and/or fall of cardiac biomarkers (preferably troponin) with at least one value above the 99th percentile of the upper reference limit together with **evidence of ischemia (with at least one of the following):**

✓Symptoms of ischemia

✓Electrocardiogram (ECG) changes (new ST changes or new left bundle branch block),

✓Development of ECG pathological Q waves

✓Imaging evidence of myocardial ischaemia

Cardiac Biomarkers

- The simple underlying principle, as with other organ markers, is that *"cell death will cause release of cellular proteins into the circulation"*

- After MI, a number of intracellular proteins are released from the damaged cells :

- **Troponins (troponin I and troponin T)**
- **enzymes (CK-MB, AST ,LDH)**
- **myoglobin.**

The Ideal Cardiac Biomarker

- ✓ *Specific*
- ✓ *Sensitive*
- ✓ *Early release*
- ✓ *Readily measurable*

Differences

1. **Distribution within the cell** → **Time to be release after cell damage**
2. **Half life in the circulation**

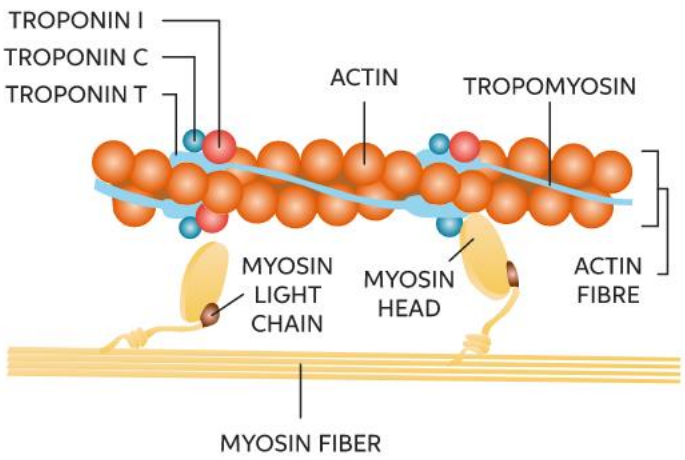
Troponins (Tn)

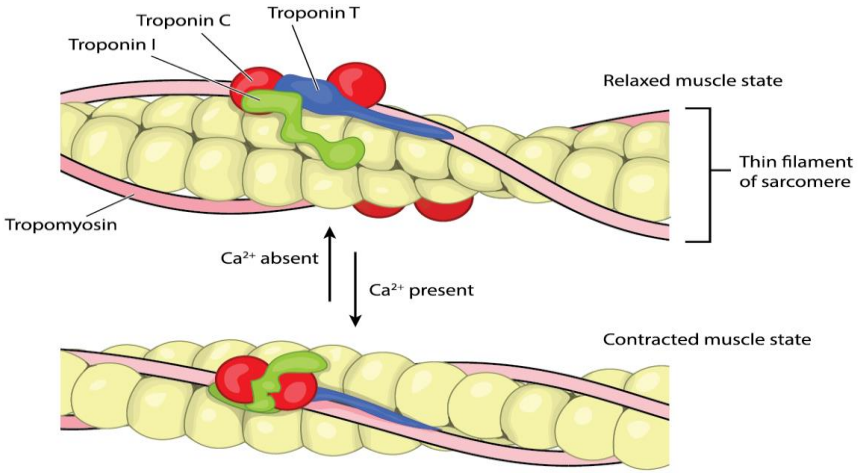
is a regulatory complex of three proteins that resides in the thin filament (Actin) of cardiac and skeletal muscle, involved in muscle contraction.

The complex is composed of:

- **TnT** attaches the complex to actin and tropomyosin molecule
- **TnI** inhibitory subunit
- **TnC** calcium-binding subunit

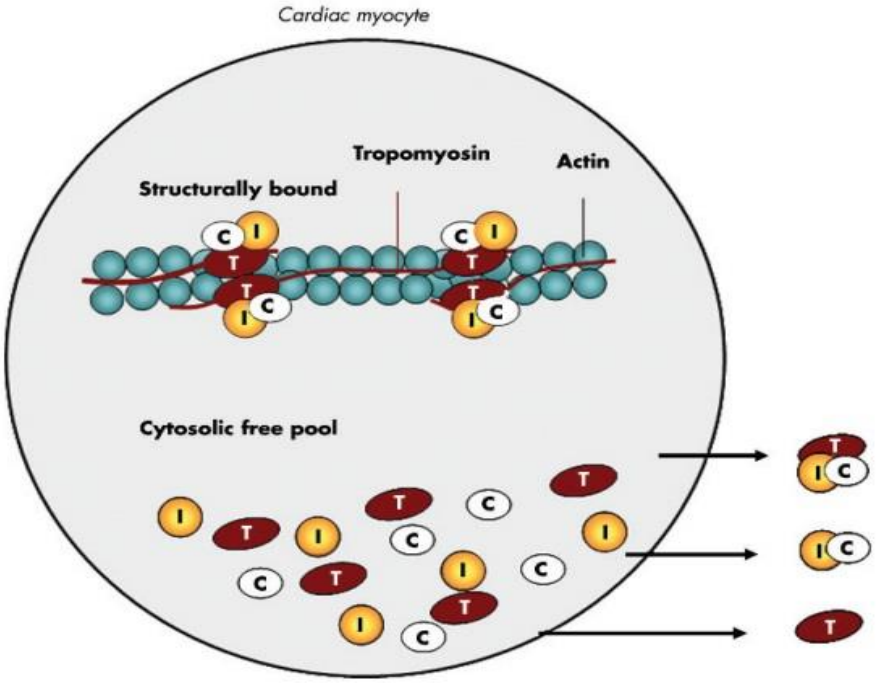
- The Ca++ trigger for muscle contraction is transmitted via the Tn complex, causing a conformational change in the thin-filament tropomyosin, allowing interaction between actin and myosin to proceed



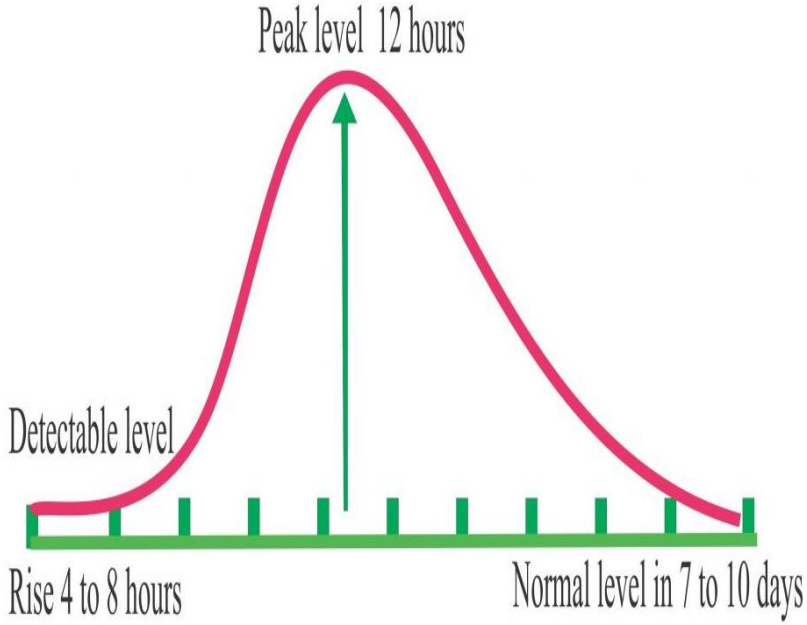


Troponin is location within the cell

- myofibrils (94% to 97%) with a smaller cytoplasmic fraction (3% to 6%)



structural (bound) form and in a free cytosolic pool. Cardiac troponins are released from myocytes as complexes or as free protein as indicated on the right.

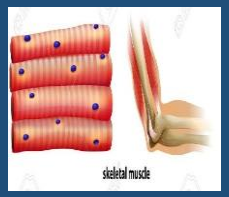


- ✓ In contrast to nearly all other muscle proteins, the forms of Tn found in skeletal and cardiac muscle differ **(different amino acid sequences as they are encoded by unique genes).**

- ✓Current gold standard for myocyte necrosis (most specific).

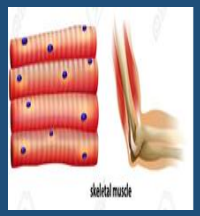
- ✓Cut-off varies with age, sex, and race.

TnC



Identical forms

TnI



Different forms

TnT

Different forms

- **TnC** the forms found in skeletal and cardiac muscle are ***identical***, thus TnC was never developed as a cardiac marker.

- **TnI** has a cardio specific form (cTnI), as well as distinct form in skeletal muscle fibers, each coded by a separate gene.

- **TnT** also has distinct forms in myocardium (cTnT) and skeletal muscle, but here the situation is more complicated, because cTnT has been detected in diseased skeletal muscle(Muscular dystrophy, polymyositis, dermatomyositis)

causes of cardiac troponin elevation in the absence of acute ischemic heart disease

- **Trauma (contusion, ablation, pacing, cardioversion)**
- **Congestive heart failure**
- **Aortic valve disease and hypertrophic cardiomyopathy with significant left ventricular hypertrophy**
- **Renal failure**
- **Drug toxicity (eg, Adriamycin, 5-fluorouracil, herceptin, snake venoms)**
- **Myocarditis**
- **Pulmonary embolism, severe pulmonary hypertension**
- **Sepsis**
- **Infiltrative disease: (amyloidosis, hemochromatosis)**

A characteristic of cardiac marker release in acute ischemic events is a rise and fall in concentration, thus, whereas most of these other conditions will demonstrate persistently raised results, the distinction can often be made by repeat measurements of troponin levels.

Creatine kinase

CK consist of two subunits, M and B which combined to form three isoenzymes :can be separated by electrophoresis

BB(CK1)

BM(CK2)

MM(CK3)

- **CKMM is predominate isoenzyme in skeletal and cardiac muscle and is detectable in the plasma of normal subjects.**

- **CK BB is present in high concentration in the brain and the smooth muscle of the gastrointestinal and genital tract, CK-BB rarely appears in plasma and has no diagnostic importance.**

- **CKMB is present in high concentration in cardiac muscle.**

➢ **As a general rule, cardiac muscle is the only tissue with more than 5% CK-MB**

Limitations of CKMB

- **False elevations in:**
  - **Skeletal muscle injury**
  - **Marathon runners**
  - **Chronic renal failure**

CK-MB FRACTION

CK-MB fraction= CKMB /total CK

CK-MB fraction greater than 2.5% is suggestive of myocardial injury

MYOGLOBIN

- Heme protein found in **cytoplasm** of cardiac & skeletal muscle cell

- **Earliest** marker of myocardial cell damage, detectable in blood within 1-2-hours of myocyte damage.

- **Not cardiac specific,** frequently elevated in presence of renal failure, skeletal muscle injury, & trauma

.

- A **negative** myoglobin result on an appropriately timed sample can be used to rule out myocardial damage and thereby determine early patient management. A **positive** result requires further investigation.

Biomarkers No Longer of Clinical Use

- LDH isoenzymes
- AST

Biomarkers of interest (although they are not currently used routinely):

Copeptin

- A 30 amino acid glycoprotein, constituting C terminal portion of arginine vasopressin
- recent studies have shown that measurement of copeptin serve as rapid and early rule out of biomarker of MI at presentation in patient with symptoms suggestive of MI .
- further additional clinical studies will be necessary

Timing Summary

TEST	ONSET	PEAK	DURATION
CK/CK-MB	4-8 hours	18-24 hours	36-48 hours
Troponins	3-12 hours	18-24 hours	Up to 10 days
Myoglobin	1-4 hours	6-7 hours	24 hours

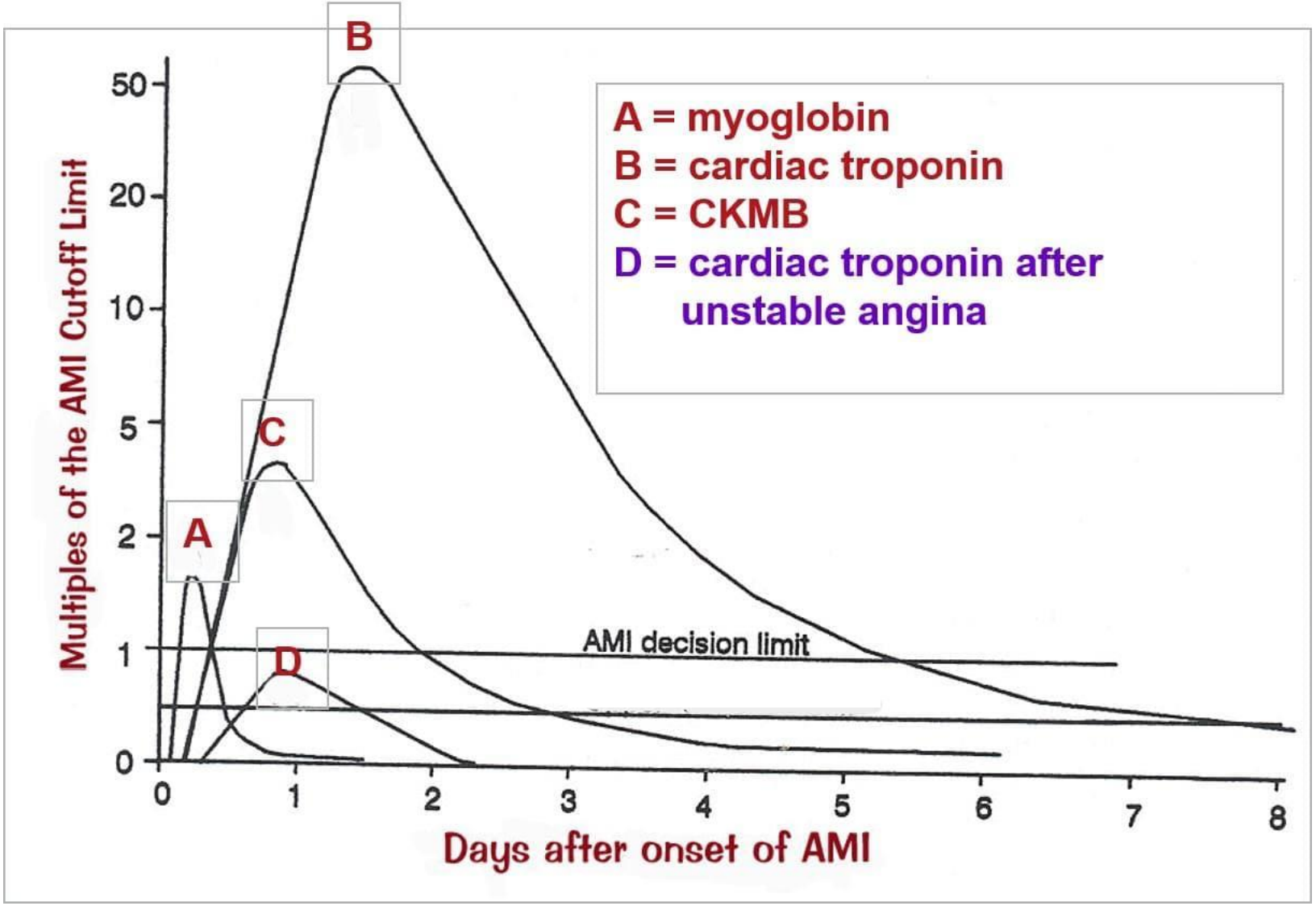
Time-course of changes

- After an MI, the time-course of plasma biochemical markers always follows the same general pattern.

- After an initial 'lag' phase, they rise rapidly to a peak between 18 - 36 h, and then return to baseline at rates that depend on the half-life of each marker in plasma.

- Patients treated by angioplasty or thrombolytic agents, the pattern is slightly modified, with a **'washout'** of markers from the infarcted area, causing an earlier peak

Marker Responses to AMI



- A 66-year-old man presented to casualty complaining of tight chest pain that had occurred 3 days previously. The pain had worsened over a few days, causing him eventually to seek medical attention.

The following laboratory test results were found:

Plasma Creatine kinase (CK) 235 U/L (< 250)

Troponin T 13.0 ng/L (< 10)

An electrocardiogram showed ST elevation in the lateral leads V4–V6.