PASSION ACADEMIC TEAM

YU - MEDICINE

Cardiovascular System

Sheet# 4 - BIOCHEMISTRY

Lec. Date :

Lec. Title : Cardiac Biomarkers

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Cardiac Biomarkers

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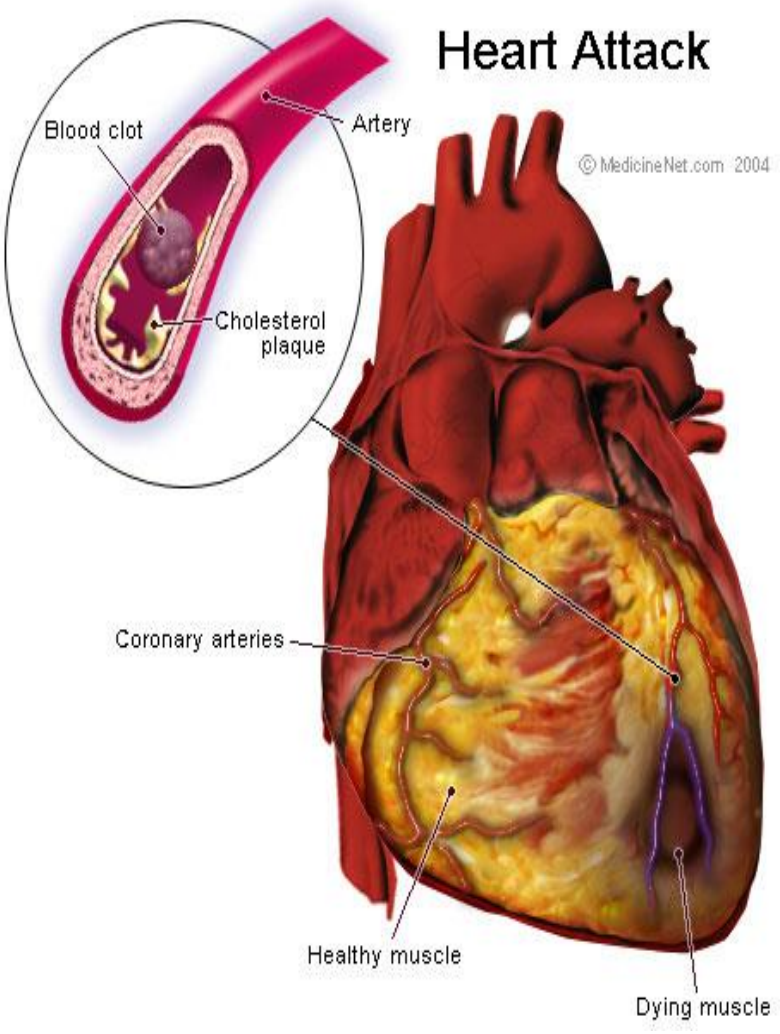
In this chapter we will talk about CVS and cardiac enzymes and cardiac biomarker .

“Cardiac markers are substances released from heart muscle when it is damaged as a result of myocardial infarction.”

❖MI is the rapid development of myocardial necrosis caused by a critical imbalance between the oxygen supply and demand of the myocardium.

❖It is an irreversible myocardial injury from prolonged ischemia.

❖Accurate and early diagnosis is important in minimizing cellular damage and, consequently, in obtaining a successful outcome for the patient

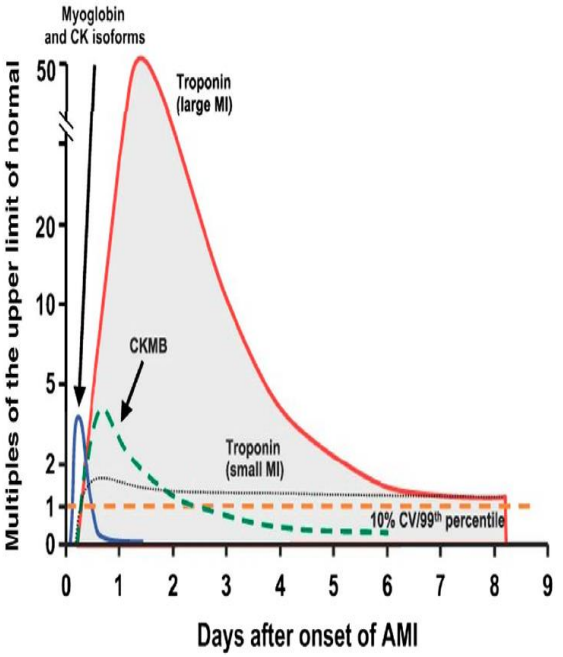


- (record)
- Cardiac biomarker can be used to diagnose myocardial infarction MI , MI can result from myocardial necrosis , when there is critical imbalance between oxygen supply and demand of myocardium , in some cases that can lead to cholesterol plaque and blood clot, hence there will be closing of arteries which leads to hypoxia condition and dead of myocardial cells , when myocardium death occur there will be release of enzyme that present in cardiac cells to blood stream, so main principle in this lecture : measurement of these enzyme which have to be in cardiac cells in the blood , if there is high cardiac enzymes in the blood that indicate to MI that is the main idea which we will focus in it

WHO- Criteria for the diagnosis of MI

1. **Ischemic symptoms (severe prolonged pain)**
2. **ECG changes consistent with ischemia**
3. **Biochemical markers (cardiac enzymes)**

*** Biochemical markers in the diagnosis of MI**



A. Early markers (they are not specific but their level is a
   after the onset) eg. Myoglobin, CK-MB

B. Definitive marker (specific, but their values elvates latter) dignostic tests: cTnI, cTnT or CK-MB

C. Old markers (total CK, CK-MB activity, LD, LD isoenzyme)

(record)

- MI can be diagnosed by many ways , one of them is biomarker , in some cases we can diagnose it by ECG changes consistent with ischemia and in some cases can diagnose it by ischemia symptoms like severe prolonged central chest Pain , all of these can give indication of MI .
- Biochemical markers are more specific tool to diagnose MI , because studies indicated that there are a lot of cases have normal ECG although having MI so only to diagnose this individual case through biomarker

- (cont..)

- -* **Biochemical markers in the diagnosis of MI**

A. Early markers (they are not specific but their level is already elevated fast about 4-6 hours after the onset) eg. Myoglobin, CK-MB

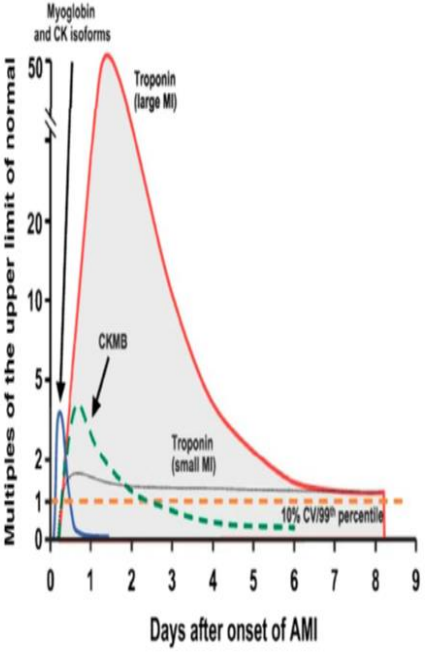
B. Definitive marker (specific, but their values elevates latter) diagnostic tests: cTnI, cTnT or CK-MB , certainly and high specific to myocardium, but their elevation in plasma can appear in later time

C. Old markers e.g (total CK, CK-MB activity, LD, LD isoenzyme)

(record " about figure that represent time since the onset of symptom appearance and cardiac enzyme activity")

-note 1 : there are early marker and later marker , if symptoms of MI per day form 0 to 1 day the first of three markers or more specific marker that can be used is troponin because its activity in plasma up to 25 x compared with individual who doesn't have MI , so troponin is early diagnose marker that can be until third or fourth or fifth day so it stills be diagnostic, so troponin used as gold standard for MI diagnosis.

Note 2 :total CK or CK-MB at 3 days they will declined for example (case): if there is person suffer from severe central chest pain from period and we make order to total CK and CK-MB test , in this case test result will be negative that doesn't mean not having MI that mean we use not proper test because we mentioned that CK and CK MB at 3 day their activity in blood circulation will declined so result will be negative , so we must use proper test that stay active in blood for 3 or 4 days like troponin.



Serum enzymes in heart diseases

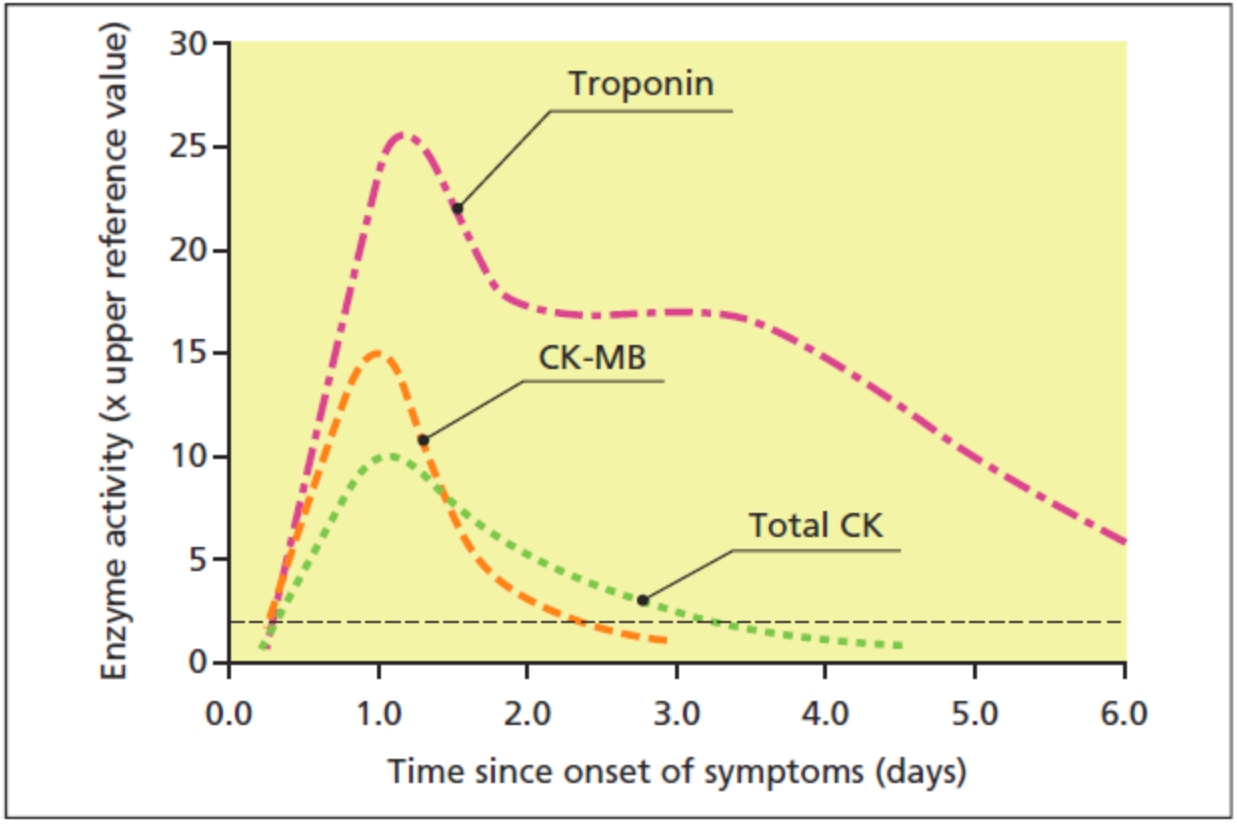
After myocardial infarction, a number of intracellular proteins are released from the damaged cells.

Important assays that are carried out in myocardial infarction are:

1. **Creatine Phosphokinase/ Creatine Kinase (CK)**
2. **Aspartate Transaminase**
3. **Lactate Dehydrogenase**
4. **Gamma- Glutamyl Transpeptidase**
5. **Pseudo-cholinesterase**
6. **Troponins**

If there is elevation of this cardiac enzymes in blood it may indicate of MI .

Usually after MI, the time –course of plasma biochemical markers always follow the same general pattern as the below figure shows



نفس شرح الرسمة السابقة ونفس الحكي

Pattern of biochemical markers in the first few days after uncomplicated MI

Table 12.1 Time-course of plasma biochemical marker elevation after myocardial infarction.

Enzyme	Abnormal activity detectable (h)	Peak value of abnormality (h)	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
'Heart-specific' LDH	8–16	30–48	5–14

Cardiac enzymes are different in abnormal activity detectable and peak and duration ....

(من الاخر الجدول مطلوب وحفظ)

1. Creatine Kinase (CK)

This enzyme catalyses the following reaction:

Creatine- phosphate + ADP -----→ Creatine + ATP

- Found in high concentration in skeletal muscle, myocardium and brain.
- The level of CK activity in the blood is due to leakage from muscle tissues.
- **After MI, serum value is found to:**
  - Increase after about 6 hours
  - Reaches a peak level in 18- 30 hours
  - Returns to normal level in 2-5 days
- Studies suggests that the serum CK activity is a more sensitive indicator in early stage of MI

(record)

-We will talk about specifity of cardiac enzymes, some of them aren't specific because they can present on myocardial cells or may present in skeletal muscles or in liver or in different types of cells , famous example pf specifity is description of three isomers of CK (creatine Kinase) , these 3 isomers are CK- MM, CK- MB , CK -BB each of them can be in specific site : **CK-MM** (Skeletal Muscle Tissue), **CK-MB** (Cardiac Muscle Tissue) and **CK-BB in** (Brain and Nerve Tissue).

- so patient with MI , we expect there will be increasing in total CK and if we do more specific test will be major elevation in CK- MB , elevation in CK MB give us indication of MI

- CK is composed of 2 polypeptide chains, B and M.
- Distribution of the three isomer forms of CK varies throughout the tissues:

- **CK-MM** (Skeletal Muscle Tissue)
- **CK-MB** (Cardiac Muscle Tissue)
- **CK-BB** (Brain and Nerve Tissue)

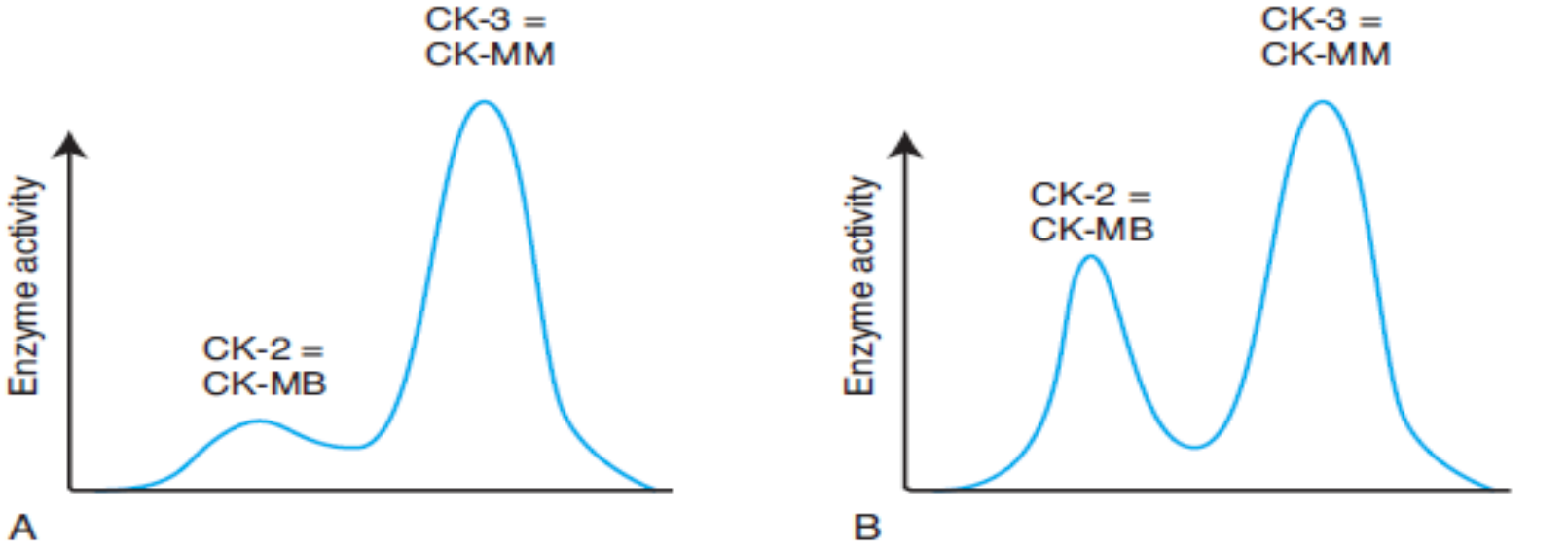


Figure 8–1. Electrophoretic separation of the CK isoenzymes in the serum of (*A*) a healthy individual and (*B*) a patient with acute myocardial infarction. Isoenzymes are numbered on the basis of their electrophoretic mobility, with the most anodal form receiving the lowest number.

(record about this figure) :
(A) : healthy individual , peak value of CK3 and CK2 in certain normal level
(B) : patient with MI , so increasing in peak value of CK2 (CK MB)
so it is considered very important test to diagnose MI for example , if there is patient had an accident car and suffer from damage in skeletal muscles then MI we will expect that there will be elevation in 2 isomers CK-MM and CK-MB , so each enzyme use to detect certain condition in certain tissue

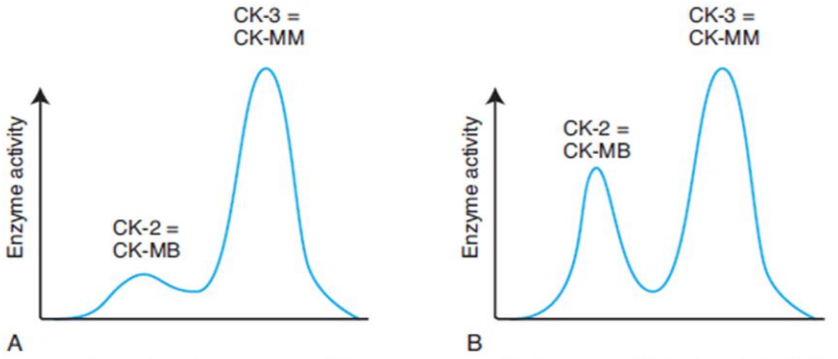


Figure 8–1. Electrophoretic separation of the CK isoenzymes in the serum of (*A*) a healthy individual and (*B*) a patient with acute myocardial infarction. Isoenzymes are numbered on the basis of their electrophoretic mobility, with the most anodal form receiving the lowest number.

Historically MI was detected by looking CK isoenzyme CK-MB.

- CK enzyme is released into circulation from necrotic heart muscle.
- As the heart muscle become damaged, CK isoenzyme is released into the blood stream and may be detected for **6-18** hours after onset of AMI.
- The window of detection is quite short, lasting no more than 12-18 hours after the heart attack occurred, because of protein degradation mechanisms that eliminate the CK-MB from the blood.
- Due to this short time frame, often the peak level of CK-MB is missed, leaving in doubt whether a heart attack has occurred or this is an indication of mild heart tissue damage or angina.

Reference Range

- **Creatine Kinase:**

Male: 46-171U/L

Female: 34-145 U/L

- **<u>CK-MB:</u>**

< 3.9% or < 5.0 µg/L

Patient with MI have elevated (higher) CK activity compared to normal individual

2. Aspartate Transaminase (S-glutamate oxaloacetate transaminase S-GOT)

- S-GOT is an intracellular enzyme involved in amino acid metabolism.
- An increased level of S-GOT in blood indicates necrosis or disease in the tissues.
- They catalyze transamination in mitochondria and cytoplasm of heart.

Aspartate + α-ketoglutarate ↔ Oxaloacetate + Glutamate

- Concentration S-GOT enzyme is very high in myocardium.

- In AMI, serum activity rises sharply within the first **12 hours**,
  With a peak level at 24 hours or over and return to normal within 3-5 days.

- Levels >350 IU/L should be considered fatal
- Elevations has been noted in absence of any ECG change
- Highest level of abnormal levels occurs on second day of infarction
- Rise depends on the size of infarction

- **Reference Range:** Serum activity of s-GOT varies from 4-17 IU/L

Not mentio ned in record

3. Lactate Dehydrogenase (LDH)

- LDH enzyme found in almost all of the body's cells and is released from cells into the fluid portion of blood when cells are damaged or destroyed.
- In AMI, serum activity rises within **12-24** hours,
- Attain peak at 46 hours, reaching about 1000 IU/L
- Returns gradually to normal from **8^{th} to 14^{th} day**
- The peak rises in LDH is roughly proportionate to the extend of injury to the myocardial tissue
- LDH elevation may persists for more than a week after CK and S-GOT levels have returned to normal levels.

- **Reference range of LDH in serum: 180-360 IU/L**
- **LD1: 14-26% of total LDH**

(record) :

LDH enzyme found in almost all of the body's cells and is released from cells into the fluid portion of blood when cells are damaged or destroyed , so LDH can give indication of MI but little bit because it is not highly specific.

More specific of LDH

LDH-1: heart and red blood cells

LDH-2: white blood cells (increases in inflammation process)

For example if there is elevation LDH and other biomarker like troponin and CK that may give us an indication of MI , but if there is just increasing in LDH 2 may be indicate to increasing of WBC due to hemolysis and different types of condition .

- *LDH-1*: heart and red blood cells
- *LDH-2*: white blood cells.
- The level of isoenzyme LDH1 compared with LDH2 has been used to detect an AMI because of the high concentration of LDH in cardiac muscle fibres.
- LD isoenzymes begin to leak out of dying heart muscle cells and are detectable in the serum by 12 to 24 hours following a heart attack.
- The appearance of more LD1 than LD2, also called 'flipped pattern', is typical of cardiac muscle damage but is non-specific since it also is associated with RBC cell haemolysis or anaemia.

الجدول مطلوب (الحالات الي بتزيد فيها ldh1/ldh2 without inflammation

Conditions causing flipped LD1/LD2 without AMI

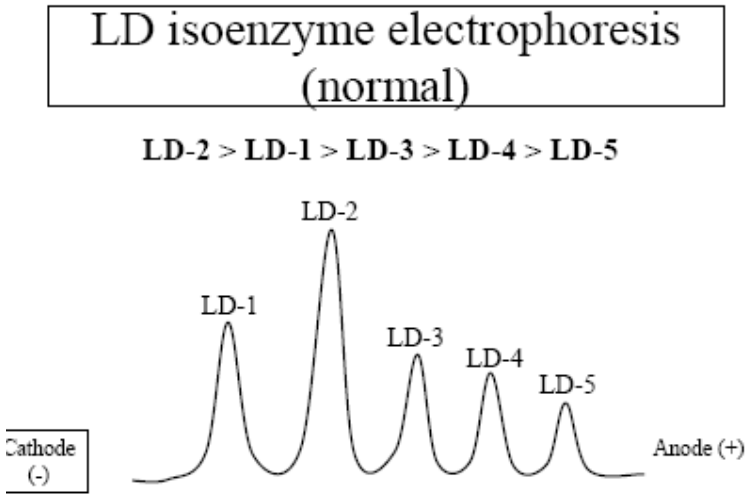
- Hemolysis
- Megoblastic Anemia
- Renal Cortex Infarction
- Testicular Germ Cell Tumors

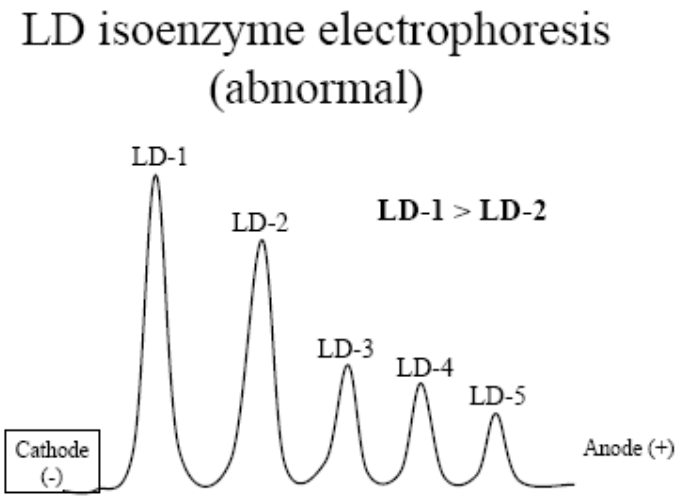
- Small Cell Lung Carcinoma
- Adenocarcinoma of the Ovary
- Acute Coronary Insufficiency (Unstable Angina)
- Exercise Induced Myocardial Ischemia
- Muscular Dystrophies

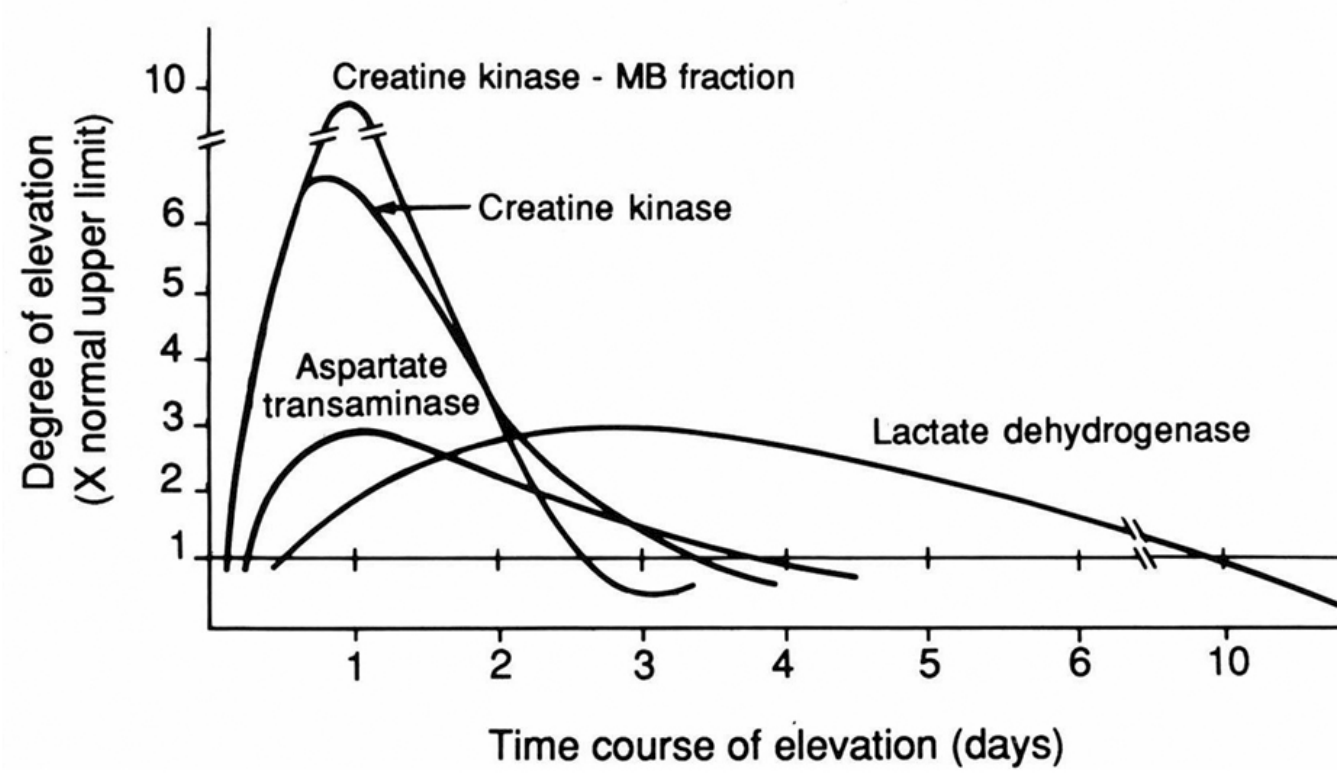
The 'flipped pattern' pattern, in which LD1 > LD2, lasts up to 3-4 days after the heart attack

Normal
LD1:LD2 = 0.5-0.75

MI
LD1:LD2 > 1







Time course of myocardial enzymes appearing in the blood after myocardial infarction

(record “ about figure “) :

-It represents the time frame of more cardiac enzymes like CK at top peak at first day and aspartate transaminase , whereas LDH optimum course elevation of its is late approximately at three days .

- So as we classified them to early marker (troponin and CK) and late like LDH according to symptoms appearance for example patient with cardiac infarction and negative ECG we can make more detect by proper test depend on symptoms appearance.

(CK , LDH, aspartate transaminase, gamma glutamyl transpeptide, histamine ,cholinesterase, troponin and myoglobin), all of these are enzyme have specific functions and their functions easly to remind as mentioned in slides , but their specific function aren't very important to remind, but you have to know that these enzymes have specific cardiac functions because they find in cardiac cells , and their activity elevation in blood circulation that gives us indication of MI . Also you have to know the types and when this markers used as early diagnosis or late to make proper diagnose for person with MI .

خلاصة المطلوب من هاي الانزيمات فما تتعمقوا بتفاصيلهم كثير اعرفوا المطلوب

4. ϒ-Glutamyl Transpeptidase

- ϒ -GTP catalyzes the transfer of the ϒ-glutamyl group from one peptide to another peptide or to an amino acid.

- Several investigators recently have demonstrated increase in serum ϒ-glutamyl transpeptidase in acute myocardial infarction. It will also get accumulated in atherosclerotic plaques

- Increase serum activity is found to be *late*, peak activity between **7th and 11th** day and lasts as long as a month. Hence it has been proposed as a useful test for **MI in later stages**.

Reference Range

- Men: 10-47 IU/L
- Women: 7-30 IU/l

5. Histaminase

- Normal plasma contains either very small amount of histaminase or none at all, but considerable amount of histaminase has been found in human heart muscle.
- Serum enzyme activity rises within 6 hours of MI and persists for whole of first week.
- It helps in early diagnosis of MI even when ECG failed to reveal.
- It also has a prognostic value as higher serum histaminase levels were found to be associated with worse prognosis.
- The reference range of Histaminase activity in adult human:
  0.12-0.76 PU/ml

6. Cholinesterase

Cholinesterases are enzymes which hydrolyze esters of choline to give choline and acid.

They are of two types:

1. *True* cholinesterase: It is responsible for destruction of acetyl choline at the neuromuscular junction and is found in nerve tissues and RB cells.
2. *Pseudo* cholinesterase: It is found in various tissues such as heart muscle and liver.

Raised activity is found within 12 hours or even as early as 3 hours found in some cases.

Serum enzyme activity has been considered as a sensitive index for determination of cellular necrosis in myocardium.

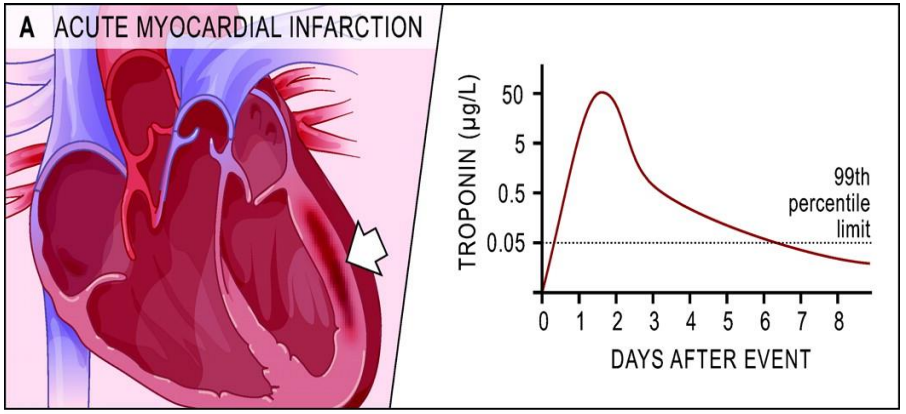
7. Troponins

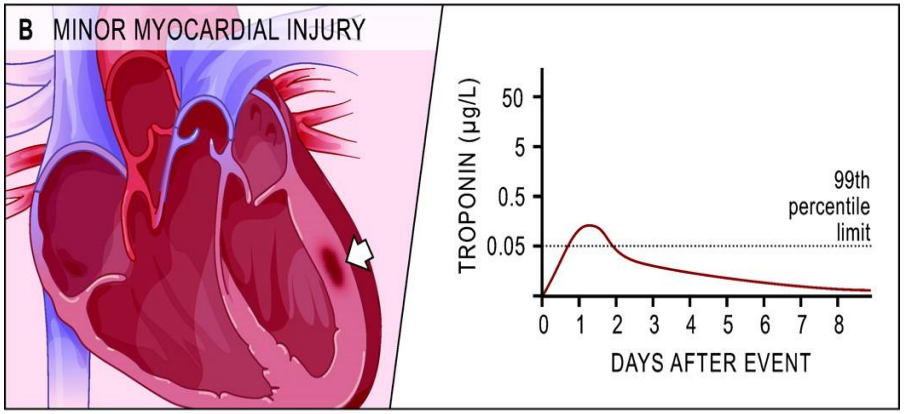
❖Troponins are protein molecules that are part of cardiac and skeletal muscle.

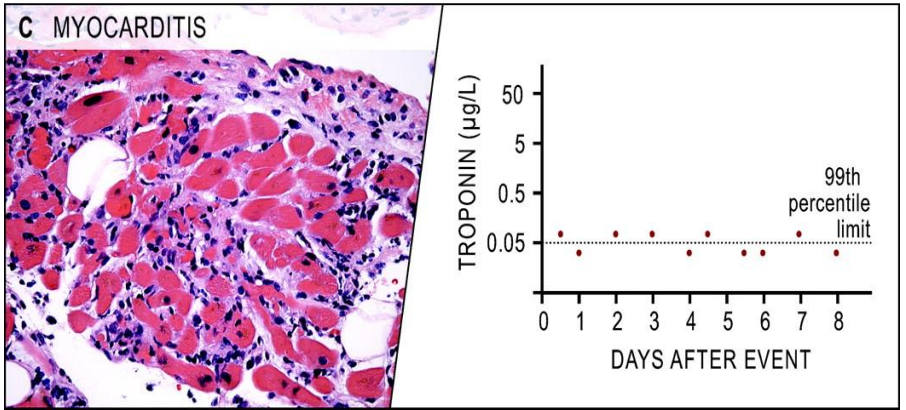
❖Smooth muscle cells do not contain troponins.

❖Troponin tests are primarily ordered to help diagnose a heart attack and rule out other conditions with similar signs and symptoms.

❖A high troponin and even slight elevations may indicate some degree of damage to the heart.



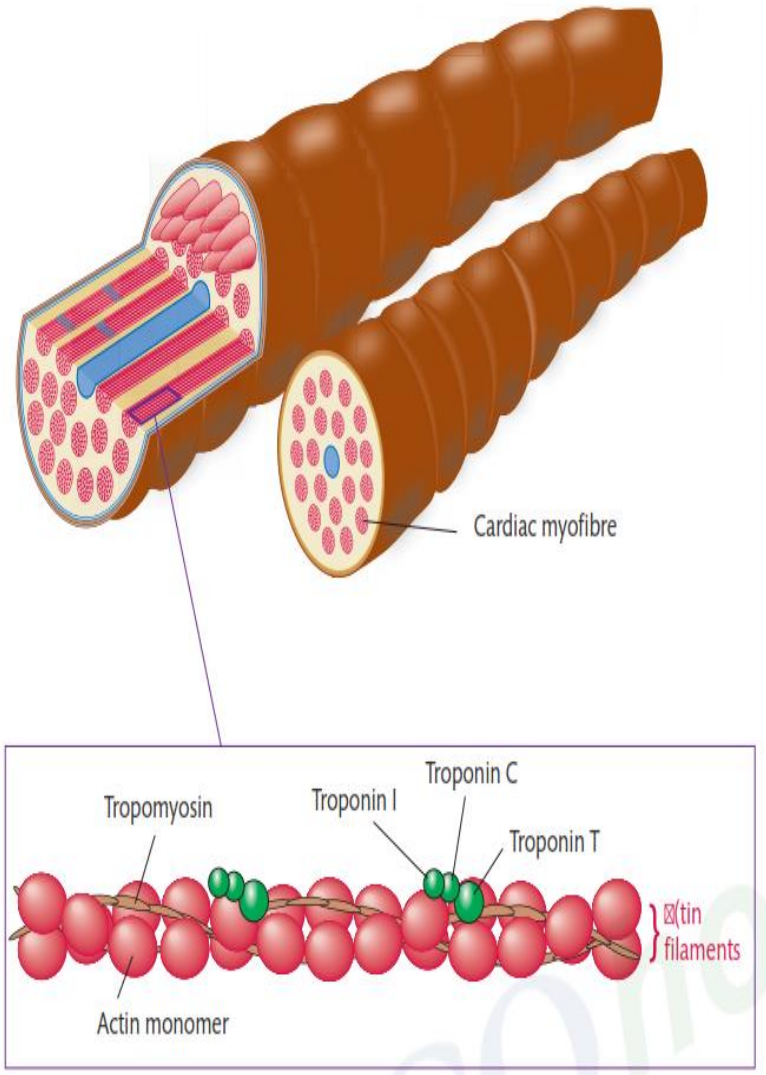




- Types of Troponin: **troponin I, troponin T, and troponin C.**

- Each subunit has a unique function: Troponin T binds the troponin components to tropomyosin, troponin I inhibits the interaction of myosin with actin, and troponin C contains the binding sites for Ca^{2+} that helps initiate contraction.

- During the process of muscle necrosis, increases in the concentration of troponins I and T above the reference levels in serum indicate heart muscle fibre and necrosis.



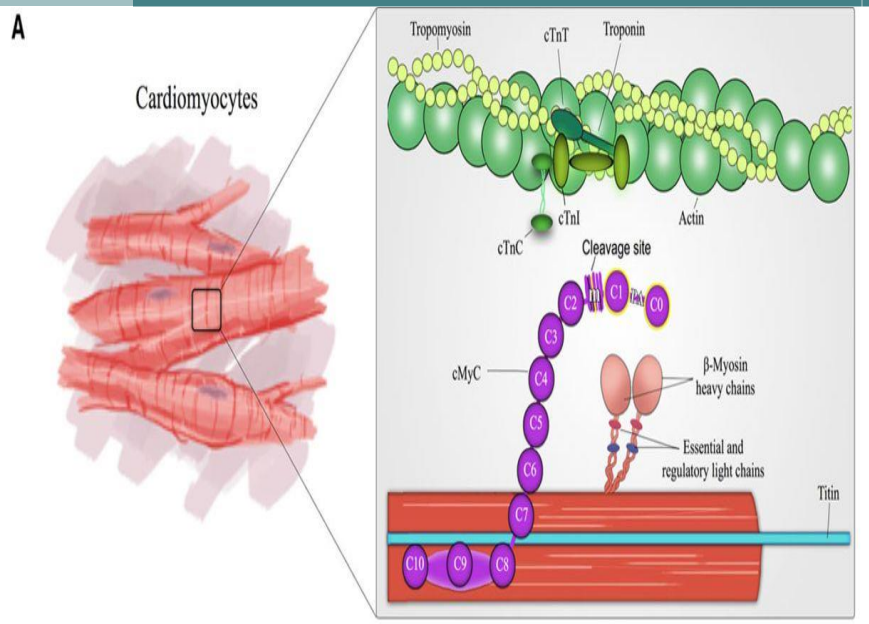
❖Troponin is the preferred test for a suspected heart attack because it is more specific for heart injury than other tests and remain elevated for a longer period of time.

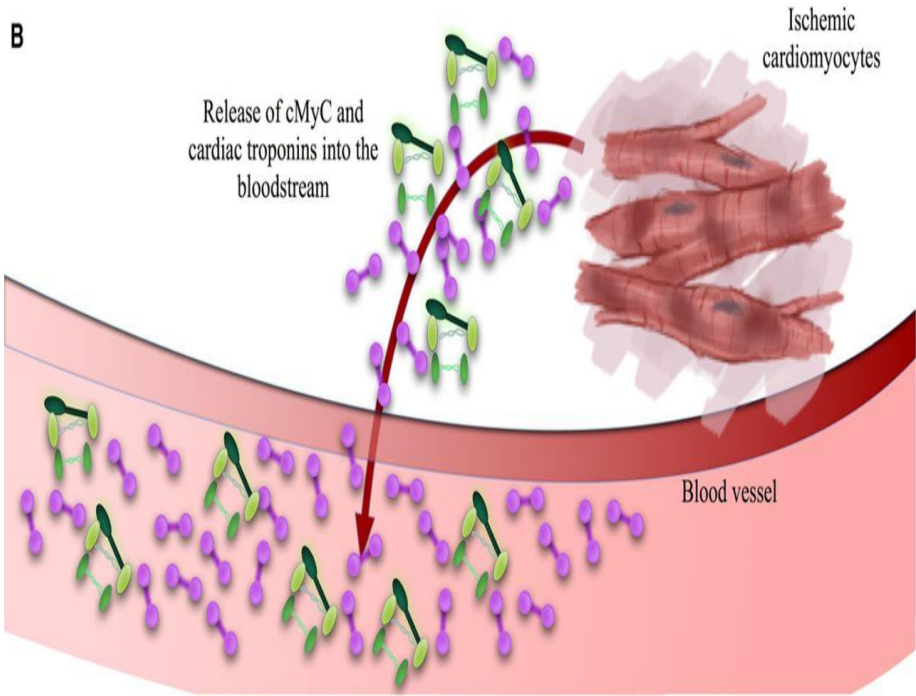
❖Troponins released from heart muscle remain in the blood stream from 1 to 14 days after the onset of AMI.

❑Troponins as cardiac markers, appear to have many advantages primarily due to their quick release following heart muscle damage and their longevity in the blood stream following heart attack

❑The risk of death from an Acute Coronary Syndrome (ACS) is directly related to troponin level.

Reference Range: Troponin I: 0.0-0.05 ng/m, Troponin T: <0.01 µg/L





8. Myoglobin

❖ **Myoglobin** is an oxygen-binding heme protein present in cardiac and skeletal muscle.

❖It increases within 2 hours post-AMI, peaks in approximately 6 to 9 hours, and becomes normal in approximately 24 hours.

❖ Many things can increase serum myoglobin levels including strenuous exercise, surgery, renal failure, and muscular dystrophy.

❖Myoglobin has high sensitivity (apper within 1 hr)but poor specificity (Skeletal muscles). It may be useful for the early detection of myocardial infarction.

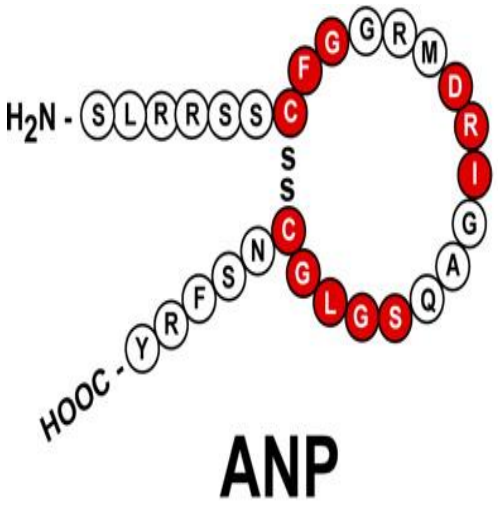
❖ Myoglobin is quickly passed by the kidneys, and elevations of it in serum may be missed if blood is not drawn appropriately.

Natriuretic Peptides

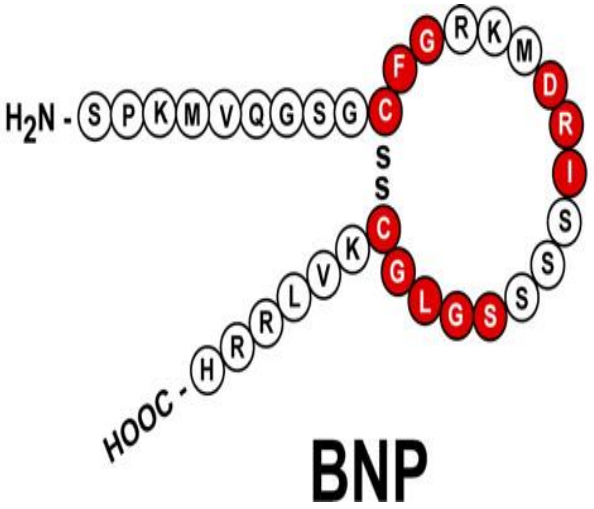
Ring-shaped molecules that promote an increased loss of sodium and water by the kidneys.

Three natriuretic peptides occur naturally:

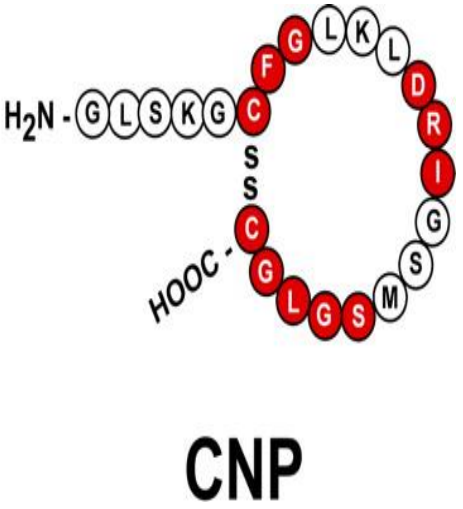
1. Atrial natriuretic peptide (ANP).
2. B type natriuretic peptide (BNP).
3. C type natriuretic peptide.



ANP



BNP



CNP

BNP and heart failure

❖Brain-type natriuretic peptide (BNP) is a neurohormone secreted by cardiac myocytes in response to volume expansion and pressure overload (excessive stretching of heart muscle cells), and plays a role in circulatory homeostasis.

❖When the left ventricle of the heart is stretched, the concentrations of BNP and NT-proBNP produced can increase markedly. This situation indicates that the heart is working harder and having more trouble meeting the body's demands

❖In heart failure the level of **BNP increases**, enabling differentiation of cardiac and pulmonary causes of breathlessness.

❖A **high** value of **BNP** in the blood: **Means** an **increased** amount of fluid or **high** pressure inside the heart.

❖It has been found that measurement of **BNP** can be reliably used to confirm or exclude a diagnosis of heart failure by general practitioners and in the emergency department.

- (record)

-Brain-type natriuretic peptide (BNP) is a neurohormone secreted by cardiac myocytes in response to volume expansion and pressure overload so, if there is excessive stretching of heart muscle cells there will be release of this neurohormone that find in wall of cardiac muscle , BNP is good indication of heart failure , if BNP is high that gives indication of HF because there is overload expansion of blood inside heart lead to release of BNP , so BNP will be find in surface area of blood circulation.

- This is different cardiac enzyme that used to diagnose HF not like other cardiac enzymes that use to diagnose MI as we mentioned , and we said that some of them are early marker and other late marker.

Cardiovascular risk factors

1. Lipid

- Lipids act as energy stores (triglycerides) and as important structural components of cells (cholesterol and phospholipids). They also have specialized functions (e.g. as adrenal and sex hormones).
- The main lipids, being insoluble in water, are transported in plasma as particulate complexes with proteins, the lipoproteins.
- From the clinical viewpoint, it is the strong relationship between plasma lipid levels and the incidence of ischaemic vascular disease, particularly of the coronary arteries

2. Cholesterol

- Cholesterol is a steroid that is present in the diet, but it is mainly synthesized in the liver and small intestine, the rate-limiting step being catalyzed by HMG-CoA reductase.
- HMG-CoA reductase inhibitors, commonly referred to as statins, are effective cholesterol lowering drugs.
- Cholesterol is a major component of cell membranes, and acts as the substrate for steroid hormone formation in the adrenals and the gonads.
- The body cannot break down the sterol nucleus, so cholesterol is either excreted unchanged in bile or converted to bile acids and then excreted.
- Cholesterol and bile acids both undergo an enterohepatic circulation.

3.Triglycerides (TG)

- TG are fatty acid esters of glycerol, and are the main lipids in the diet.
- TG are broken down in the small intestine to a mixture of monoglycerides, fatty acids and glycerol. These products are absorbed, and TG are resynthesised from them in the mucosal cell.
- Most of these exogenous triglycerides pass into plasma as chylomicrons.
- Endogenous triglyceride synthesis occurs in the liver from fatty acids and glycerol.

Lipid Profile Test				
	Unit	Optimal	Intermediate	High
Total Cholesterol	mg/dL	<200	200 - 239	>239
	mmol/L	<5.2	5.3 - 6.2	>6.2
LDL Cholesterol (calculated)	mg/dL	<130	130 - 159	>159
	mmol/L	<3.36	3.36 - 4.11	>4.11
HDL Cholesterol	mg/dL	>60	40 - 60	<40
	mmol/L	>1.55	1.03 – 1.55	<1.03
Triglycerides	mg/dL	<150	150 - 199	>199
	mmol/L	<1.69	1.69 - 2.25	>2.25
Non-HDL-C (calculated)	mg/dL	<130	130 - 159	>159
	mmol/L	<3.3	3.4 - 4.1	>4.1
TG to HDL ratio (calculated)	mg/dL	<3	3.1 – 3.8	>3.8
	mmol/L	<1.33	1.34 – 1.68	>1.68

Serum Lipids and Lipoproteins

In human, principal lipids that have metabolic significance are as follows:

1. **Triglyceride** (**TG**)
2. Phospholipids
3. Steroids
4. Fatty Acids
5. Glycerol

What are lipoproteins?

Water insoluble TG, saturated fatty acids, cholesterol and its esters are transported in the plasma as water-miscible LIPOPROTEINS (Conjugated Proteins)

- (record)

-lipoproteins : are carrier of simple lipid , Water insoluble TG, saturated fatty acids, cholesterol and its esters are transported in the plasma as water-miscible LIPOPROTEINS (Conjugated Proteins)

- they are classified depending on size , Chylomicrons the biggest and low density and there are VLDL , LDL (bad cholesterol) , HDL (good cholesterol) , all of them gave specific value .

- HDL is good cholesterol its function cleaning of arteries and remove bad TG and bad product and take them to liver in order to degradation, so increasing of HDL is good for health , whereas LDL causes accumulation in arteries and plaque formation that lead to occlusion of vessels which can cause hardening , atherosclerosis, clot that can go to many site and cause MI, stroke, heart attack ..

The four types of lipoproteins are:

1. Chylomicrons
2. VLDL
3. LDL
4. HDL

نفس الحكي

The Cholesterol form most associated with cardiovascular problems when in excess LDL.

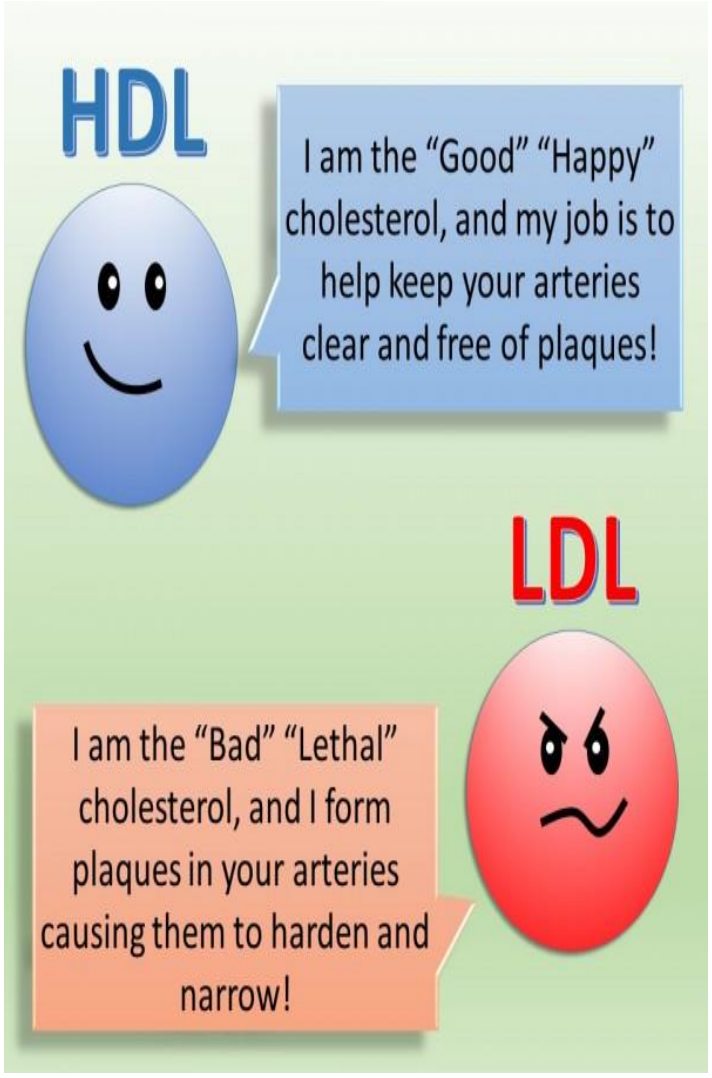
While LDL is considered harmful when in excess, the elevation of HDL is viewed as a positive cardiovascular biomarker for a patient.

Elevated HDL has a beneficial effect for the vascular system due to the role that HDL plays in the body.

HDL removes excess cholesterol from tissues and routes into the liver for reprocessing or removal

Major functions of Lipoproteins

1. **Chylomicrons**: transport mainly TG from either food or synthesised in enterocytes, also small amount of PL, cholesterylesters and fat-soluble vitamins from the intestine to liver, adipose tissues and muscles.
2. **VLDL**:- transport mainly endogenous TG, synthesized in hepatocytes, from liver to extrahepatic tissues, mainly adipose tissues for storage.
3. **LDL**:- rich in cholesteryl esters, mainly transports cholesterol and its esters from hepatocytes to extrahepatic tissues.
4. **HDL**:- transports cholesterol and its esters from extrahepatic tissues to the liver.



Total cholesterol	
Desirable	Below 200
Borderline high	200-239
High	240 or above
LDL (bad) cholesterol	
Optimal	Below 100
Near/above optimal	100-129
Borderline high	130-159
High	160-189
Very High	190 or above
HDL (good) cholesterol	
High (higher is better)	60 or above
Low	Below 40
Triglycerides	
Normal	Below 150
Borderline high	150-199
High	200-499
Very high	500 or above

- Lipoprotein(a), is a unique among the lipoproteins. It is thought to be an unusual type of LDL particle with an Apoprotein ‘a’ is covalently attached to the Apoprotein B by a disulfide bridge. It is a modified form of LDL.
- Because there is variability in the structure of apoprotein ‘a’, it is very difficult to assay and detect all the possible variants.

- Uniqueness of the Lipo(a), is also related to its similarity to plasminogen.

- Plasminogen, when converted to plasmin in the blood, is instrumental in degrading the incidental clots that are formed periodically in blood vessels.

- When plasmin is not available, little clots become big ones and can lead to blood vessel occlusions.

- High lipo(a) level inhibit plasmin formation by attracting the plasminogen activators and blocking their action

- Thus, high levels of Lipo(a) are an independent risk factor for patients. If patients have elevated levels of Lipo(a), their blood tends to clot.

- The apoprotein (a) chain contain 5 cystein rich domains known as ‘Kringles’. The 4^{th} kringle is homologous with fibrin-binding domain of plasminogen, a plasma protein that dissolves blood clots when activated.

- Because of this structural similarity to plasminogen, lipo(a) interferes with the fibrinolysis by competing with plasminogen activation, plasmin generation and fibrinolysis.

- This promotes the deposition of cholesterol as atherosclerotic plaques.

Primary and secondary hyperlipoproteinemia

Elevation of LDLs can result from inborn errors of metabolism, such as enzyme or apoprotein deficiencies or from secondary causes or underlying diseases.

Some of the diseases and medications that can cause hyperlipoproteinemia includes DM, BP medications, nephrotic syndrome, chronic renal failure, hepatic disorders including biliary obstruction.

Plaque build-up and blockage of blood vessels from excessive LDL level can occur and lead to coronary heart diseases.

Hypoalphalipoproteinemia

The absence or a non-detectable level of apoprotein A-I is exhibited by a severely decreased or absent level of HDL (Tangier's disease/ hypoalphalipoproteinemia).

This condition leads to elevated LDL in the circulation with no viable HDL action to remove cholesterol from the tissue.

Apoprotein A-I is the major apoprotein associated with HDL and is necessary for the enzyme *lecithin-cholesterol acyltransferace* (LCAT) to function. LCT joins a fatty acid to cholesterol, an alcohol, to make a cholesterol ester. These cholesterol esters can be packed into the HDL particles for transport to the liver, causing the HDL particle to go from disk shape to spherical shape in the circulation.

When Apoprotein A-I is absent, LCAT is unable to function and esterification of cholesterol is diminished.

Plaque build-up and blockage of blood vessels from excessive LDL levels can occur and lead to coronary heart diseases. Heart ailments related to hypoalphalipoproteinemia include atherosclerosis, MI and strokes.

CASE 12.1

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

Comment on these results. Has he suffered a myocardial infarction?

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

CASE 12.2

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.

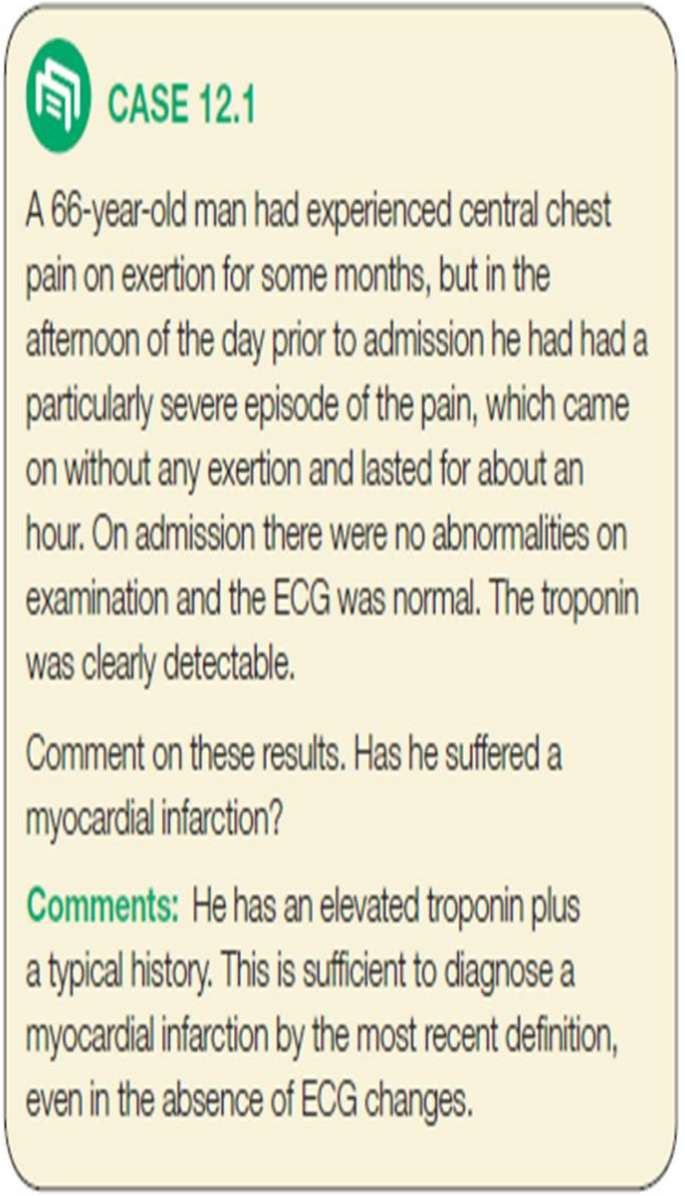
Comments: The total CK is substantially elevated, and CK-MB >6% can usually be taken to mean that it is of myocardial origin. However, the normal ECG and troponin are both reassuring. In trained endurance athletes, the proportion of CK-MB in muscle increases from the normal low levels and may be as high 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.

- (record) :

In this chapter we will discuss many cases : كلهم مطلوبين

Case 12.1 : (discussion)

66 old man suffers from central chest pain with normal ECG ,but it has troponin elevation so that give indication of MI regardless ECG normal.



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(record) :

This case give flexibility in cardiac enzymes topic , here total CK elevated and CK MB normally <6% , but here 14% so person may have MI ,but it has normal ECG and undetectable troponin which is more specific test , so person may not have MI , because in some cases a well trained marathon runner will have increasing CK as (10-15)% so this increasing doesn't indicate to MI , but this elevation due to highly demand on the heart muscle , and increase CK MB due to extreme exercise.

But if it has normal ECG and positive troponin test that indicate to MI .

CASE 12.2

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CASE 12.3

A 28-year-old man requested cholesterol testing because his father had died of a myocardial infarction in his thirties, his paternal grandfather had developed angina in his early forties and died suddenly in his late forties, presumably of an infarction, and there was a further history of ischaemic heart disease at a young age in his more extended family. The GP noted that he had tendon xanthomas on his knuckles and on his Achilles tendons. He took plenty of exercise, followed a healthy diet and was not overweight, did not smoke and was normotensive.

Comment on the history and the following results:

Serum	Result	Reference range
Cholesterol	10.6	mmol/L
Triglyceride	1.4	0.6–1.7 mmol/L
HDL	1.9	0.5–1.6 mmol/L
Cholesterol : HDL	5.6	
LDL cholesterol	8.1	mmol/L

Comments The family history and lipid results make familial hypercholesterolaemia the likely diagnosis here, and this is confirmed by the finding of tendon xanthomas. These are accumulations of cholesterol on the tendons, which are virtually pathognomonic of familial hypercholesterolaemia. The exercise he took probably accounted for the slightly high HDL, giving him an apparently quite favourable cholesterol : HDL ratio. This, with his relatively young age, the fact he did not smoke and his normal blood pressure, would give him a relatively satisfactory calculated cardiovascular risk. However, these calculations do not apply in patients with familial hypercholesterolaemia, who are at a considerably higher than calculated risk. He merits treatment with lipid-lowering drugs.

CASE 12.4

A 33-year-old man was referred to the lipid clinic with a cholesterol of 10.2 mmol/L. He had a vague memory of having his cholesterol checked at a medical examination at work in his early twenties, and thought it had been normal at that time. He had been dieting for the last few months and had succeeded in losing ~3 kg, but his cholesterol had not changed. Over the preceding 2 years he had felt tired, and stressed by his work. His GP felt that he was depressed, and had been treating him with anti-depressants with little benefit. He had stopped playing football, and his muscles ached on exertion. He had put on 20 kg over this period.

Comment on the following results:

Serum	Result	Reference range
Cholesterol	10.2	mmol/L
Triglyceride	1.1	0.6–1.7 mmol/L
HDL	1.0	0.5–1.6 mmol/L
TSH	256	0.2–4.5 U/L
FT4	<6	9–21 pmol/L
CK	12 330	30–200 U/L
Na	129	132–144 mmol/L

Comments: He has an extremely high [cholesterol] which has not improved with diet, and if his recollections were accurate had previously had a normal [cholesterol]. This raises the question of a secondary hypercholesterolaemia. He has certainly put on weight, which may increase lipids, but not usually to this extent. His symptoms of weight gain, tiredness and depression raised the possibility of hypothyroidism, and this was confirmed by his profoundly hypothyroid thyroid function tests. Hypothyroidism can also cause a myopathy, with aching muscles and very high CK, and a dilutional hyponatraemia. He thus had a full range of the biochemical abnormalities that may be seen in hypothyroidism! Treatment with thyroxine resulted in a dramatic improvement in all his symptoms apart from the muscle aching, which still persisted 6 months later. [Cholesterol] came down to a satisfactory 4.6 mmol/L without the need for any lipid-lowering medication. CK and sodium returned to normal.