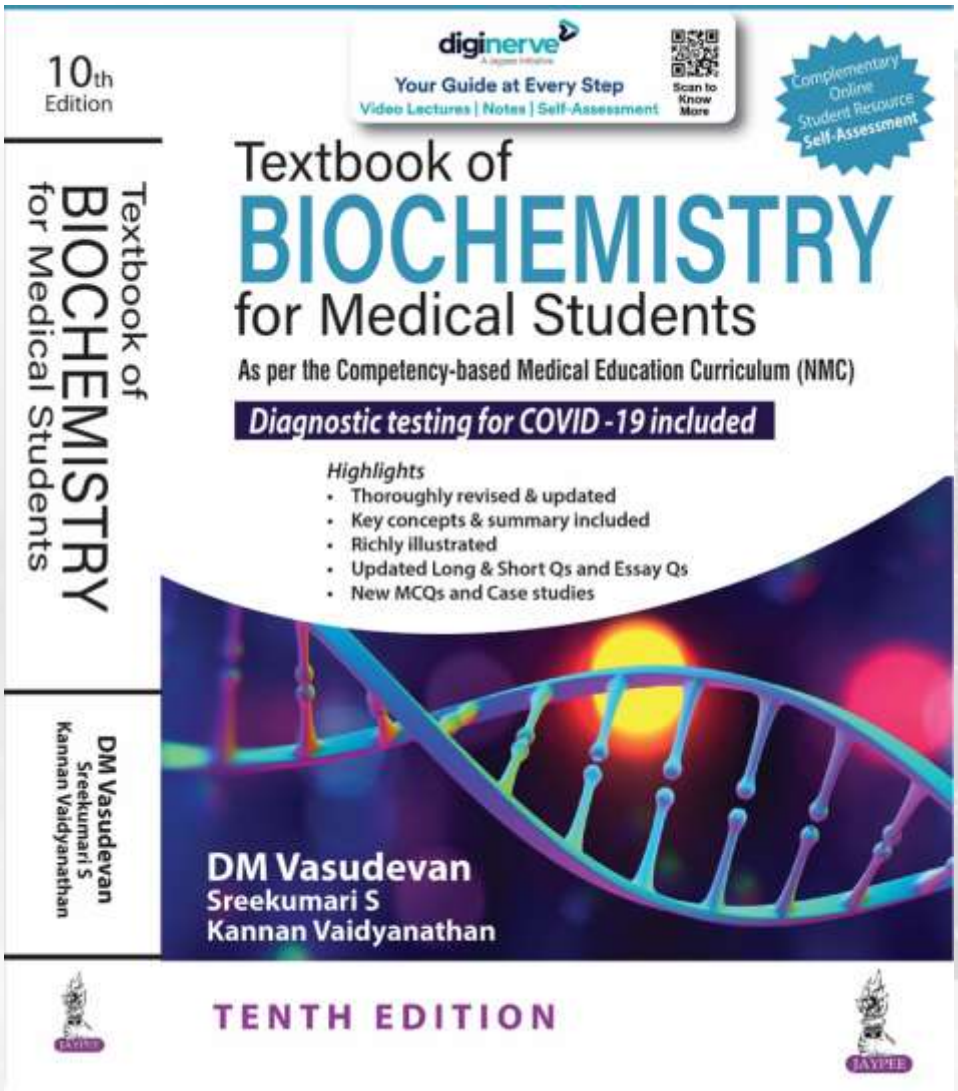


Chapter 13:

Cardiovascular disease and Biomarkers of CVD

Textbook of
BIOCHEMISTRY
for Medical Students

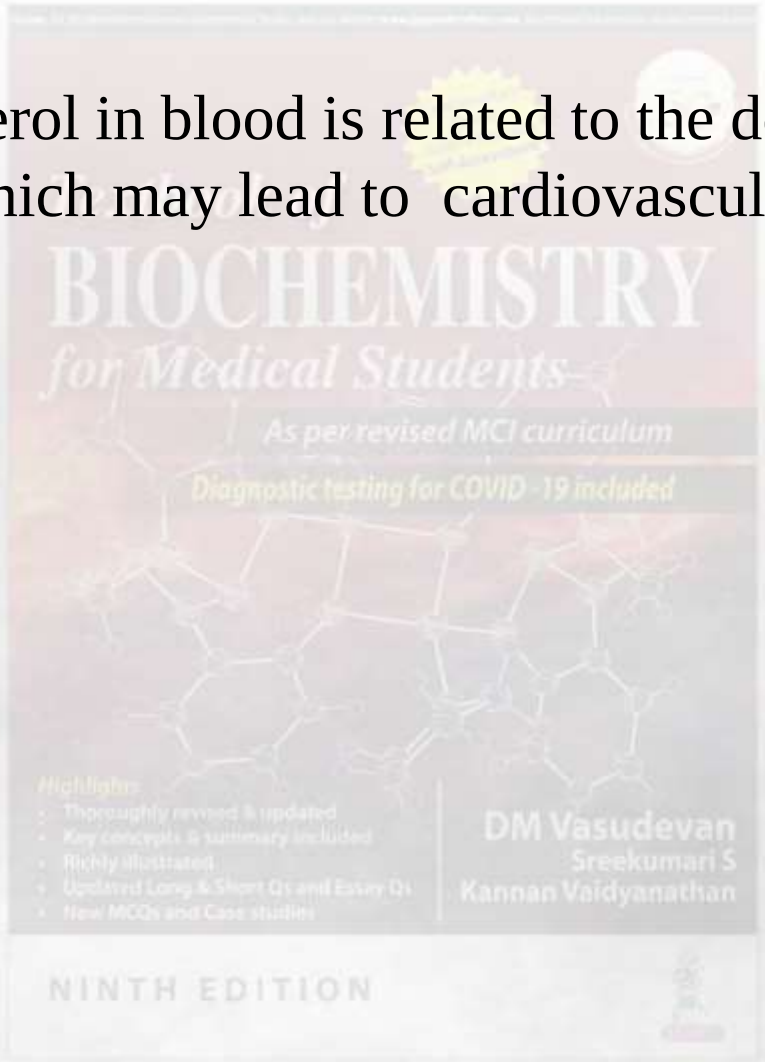
By DM Vasudevan, *et al.*

TENTH EDITION

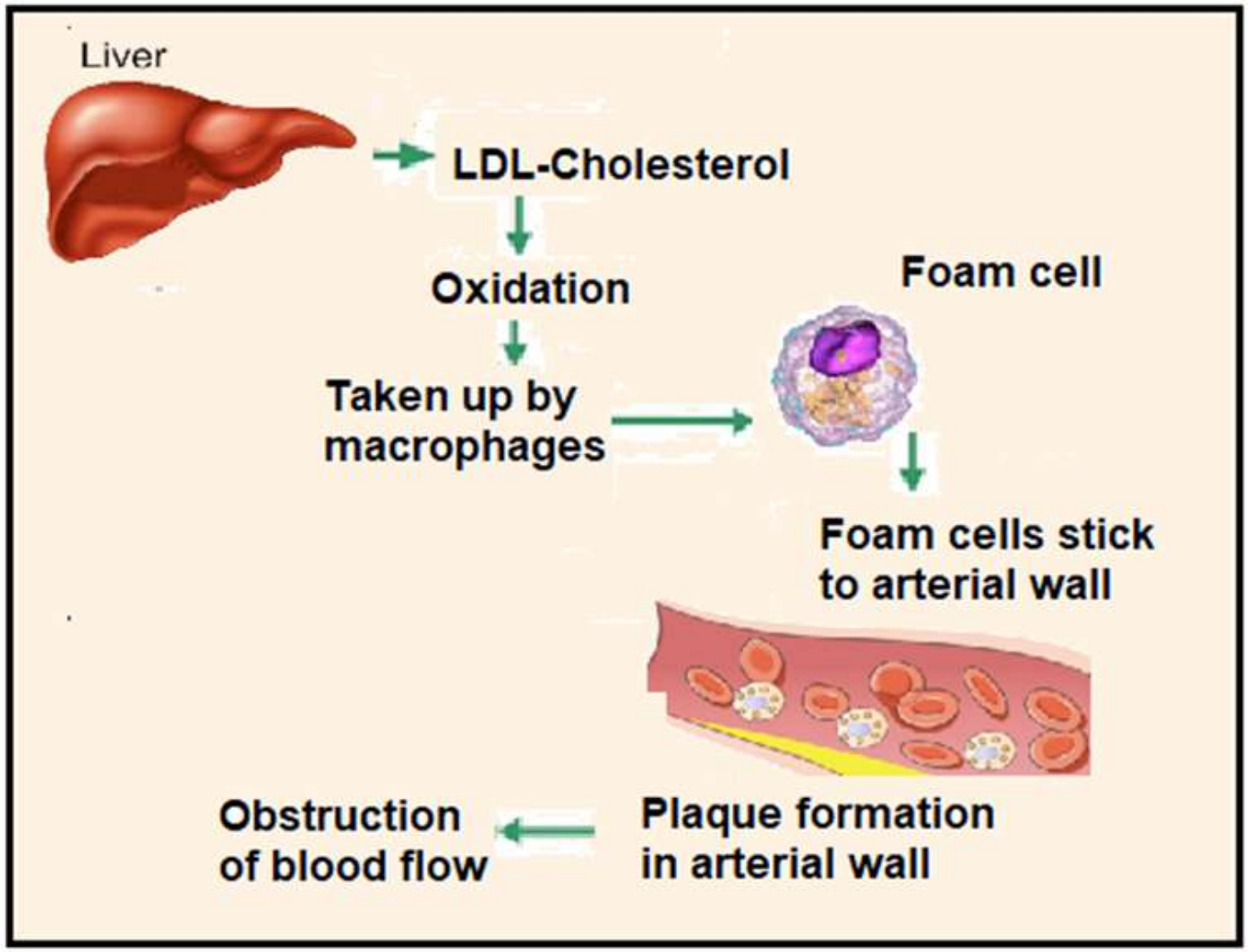
Clinical Significance of Cholesterol

Heart diseases:

The level of cholesterol in blood is related to the development of atherosclerosis which may lead to cardiovascular accidents and heart attacks.



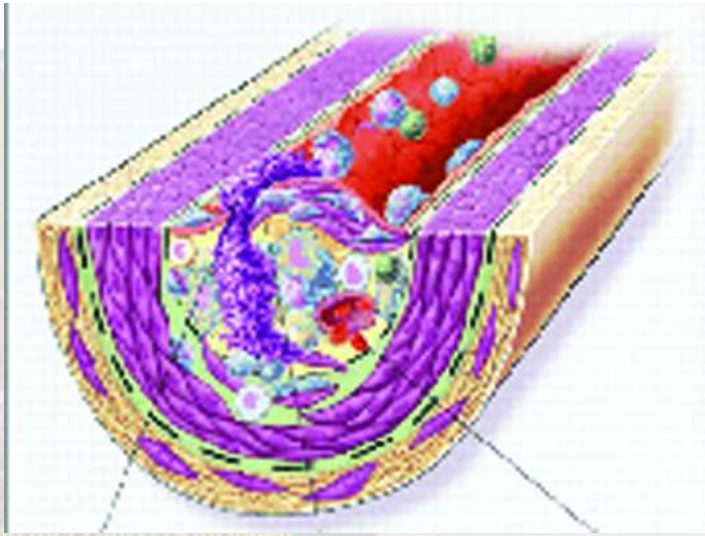
Atherosclerosis



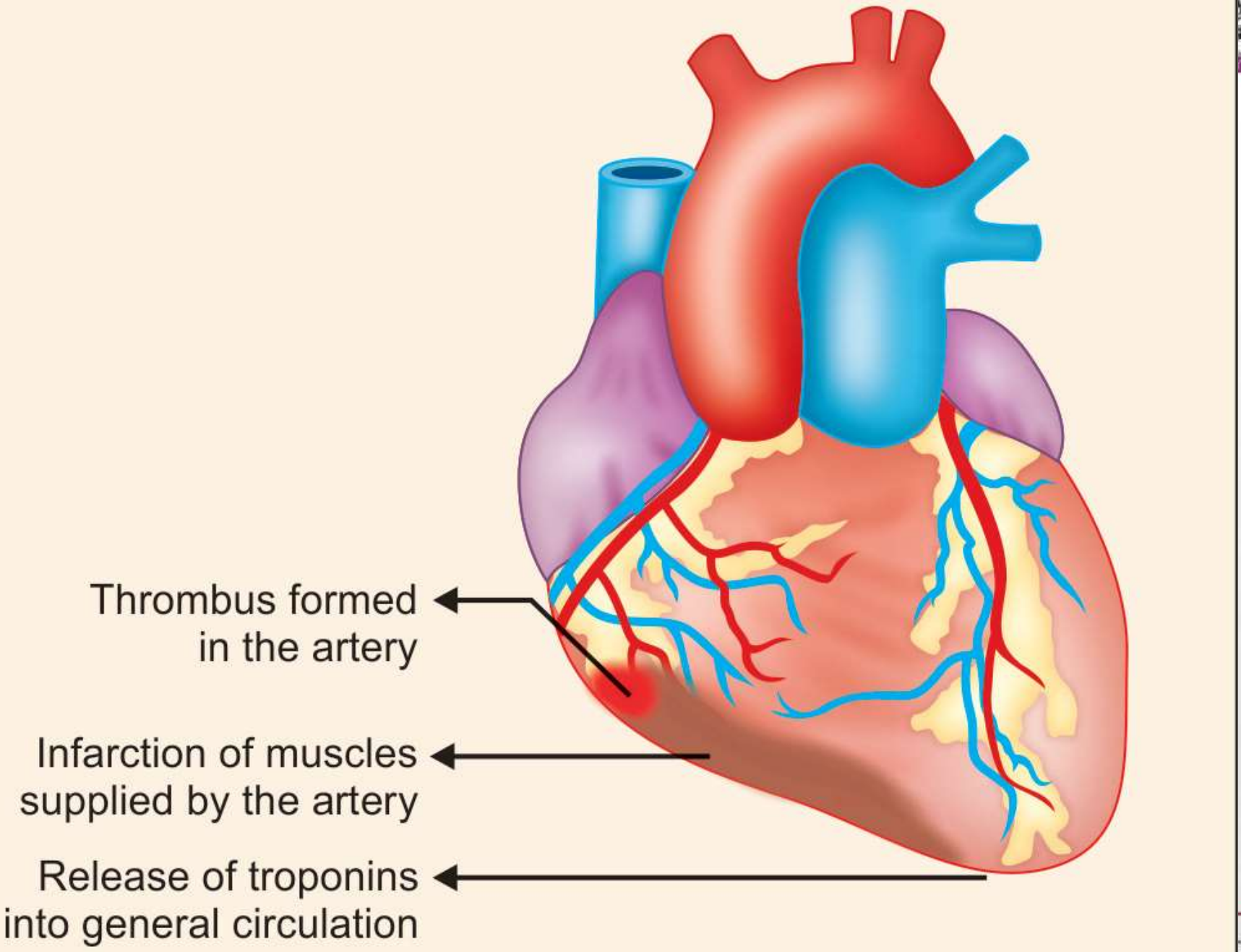
Stage I : Formation of foam cells: The LDL cholesterol, especially oxidised LDL particles are deposited in the walls of arteries.

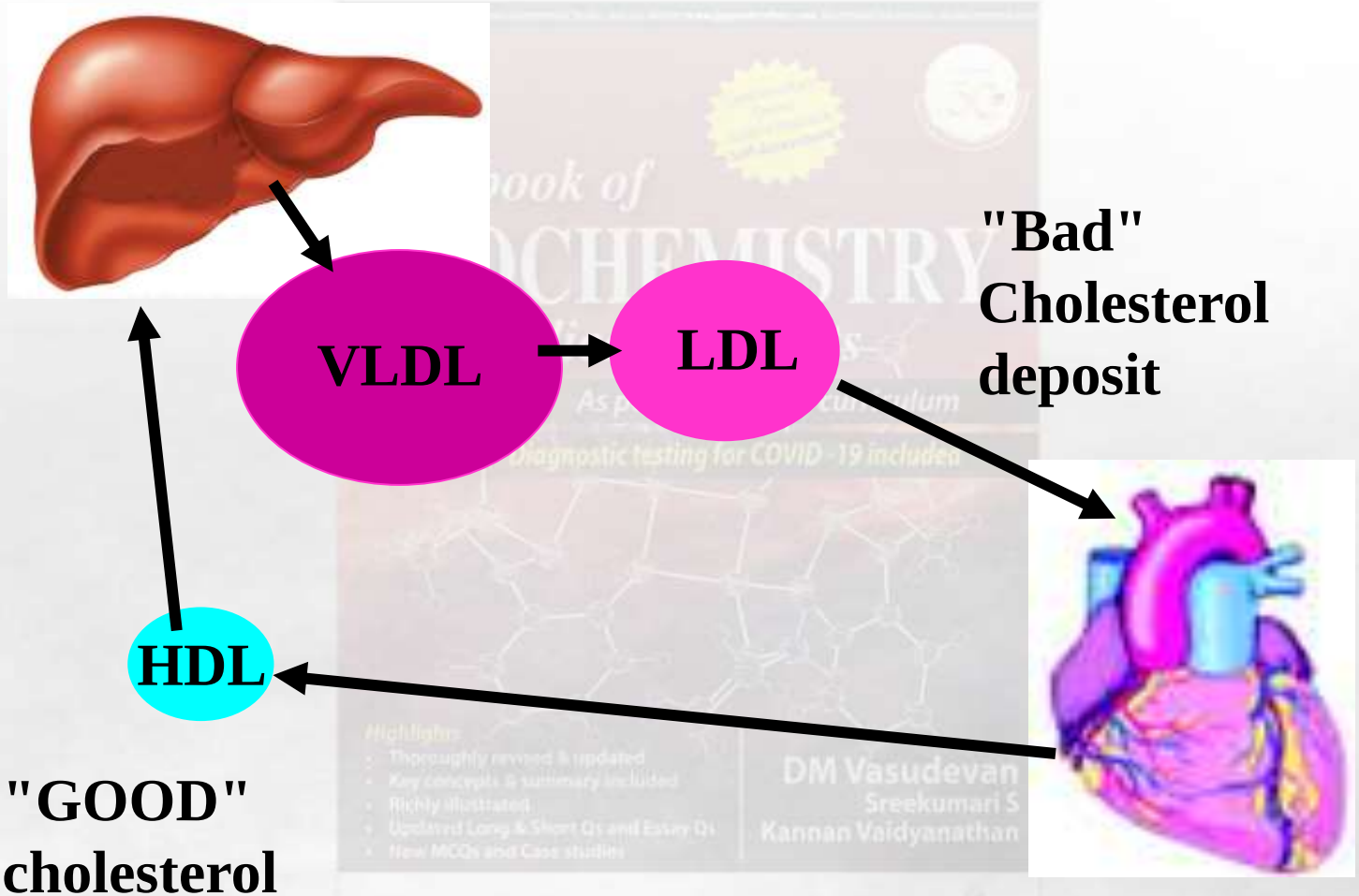
Stage II: Progression of atherosclerosis: Lipid droplets are seen in the lesion.

Stage III: Fibrous proliferation: Thus there is a definite component of inflammation in atherosclerosis. This chronic infection leads to increased hs-CRP



Stage IV: This leads to narrowing of vessel wall when proliferative changes occur. The blood flow through the narrow lumen is more turbulent and there is tendency for clot formation.


Thrombus formed in the artery
Infarction of muscles supplied by the artery
Release of troponins into general circulation


VLDL
LDL
"Bad"
Cholesterol
deposit
HDL
"GOOD"
cholesterol
(Excretion)

Classification of cardiac markers

A. Cardiac markers of myocardial infarction (MI)

Serial estimation of the following cardiac markers is usually done to assess the progress of the ischemic process. No single marker can successfully identify or exclude acute MI within the first 6 hours.

1. Cardiac troponins (cTnT and cTnI)
2. High sensitivity troponin (hs-cTnT and hs-cTnI)
3. Creatine kinase isoenzyme (CK-MB)
4. Myoglobin
5. Lactate dehydrogenase (LDH) and aspartate aminotransferase (AST) were previously used as markers of myocardial function, but not used nowadays

Classification of cardiac markers, continued

B. Markers of risk prediction

1. Total cholesterol level in serum
2. LDL cholesterol and Apo B-100 level
3. HDL cholesterol and Apo A-1 level
4. Lp(a) level
5. Serum triglycerides
6. Plasma hs-CRP
7. Blood HbA1c level in diabetes mellitus
8. Serum homocysteine level
9. Lipoprotein-associated phospholipase A2

C. Markers of myocardial stress

1. BNP and NT-proBNP. It is a reliable marker of ventricular function.
2. Adrenomedullin
3. Copeptin

Cardiac Biomarkers

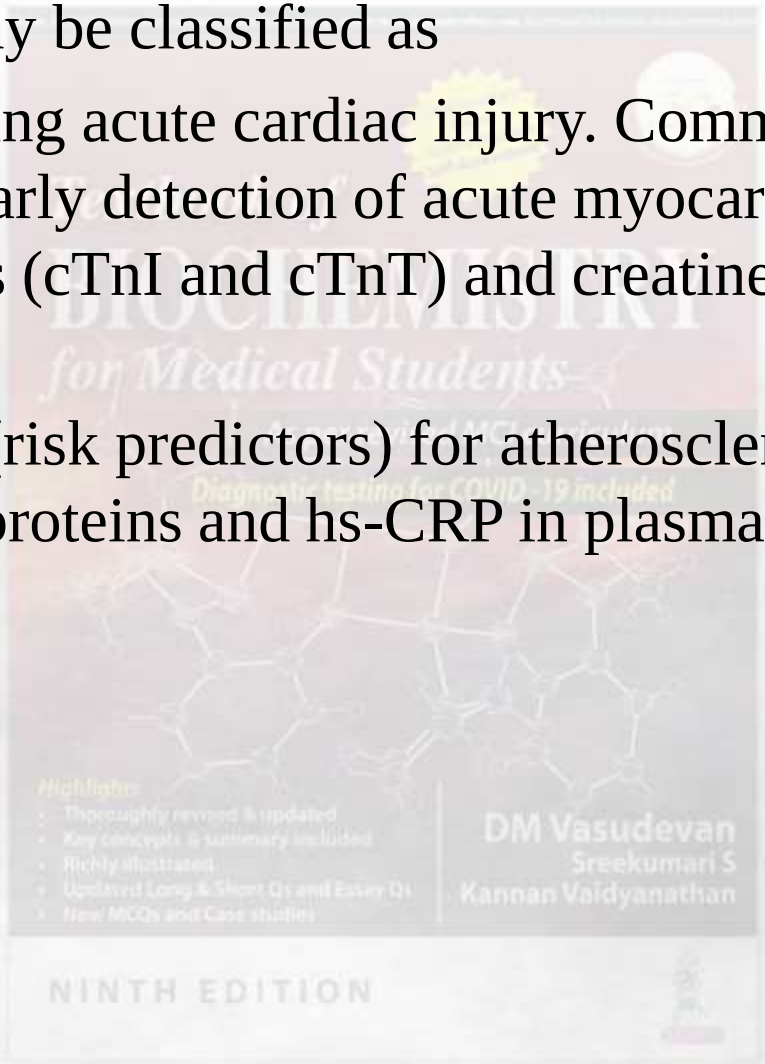
A biomarker is defined as one naturally occurring molecule, gene, or characteristic by which a particular pathological process or disease can be identified.

Another definition is that a biomarker is a substance used as an indicator of the presence of a material of biological origin, of a specific organism, or a physiological condition or process; specifically a diagnostic indicator of a medical condition.

In simple terms, a biomarker is a substance that can be used as an indicator of a particular disease.

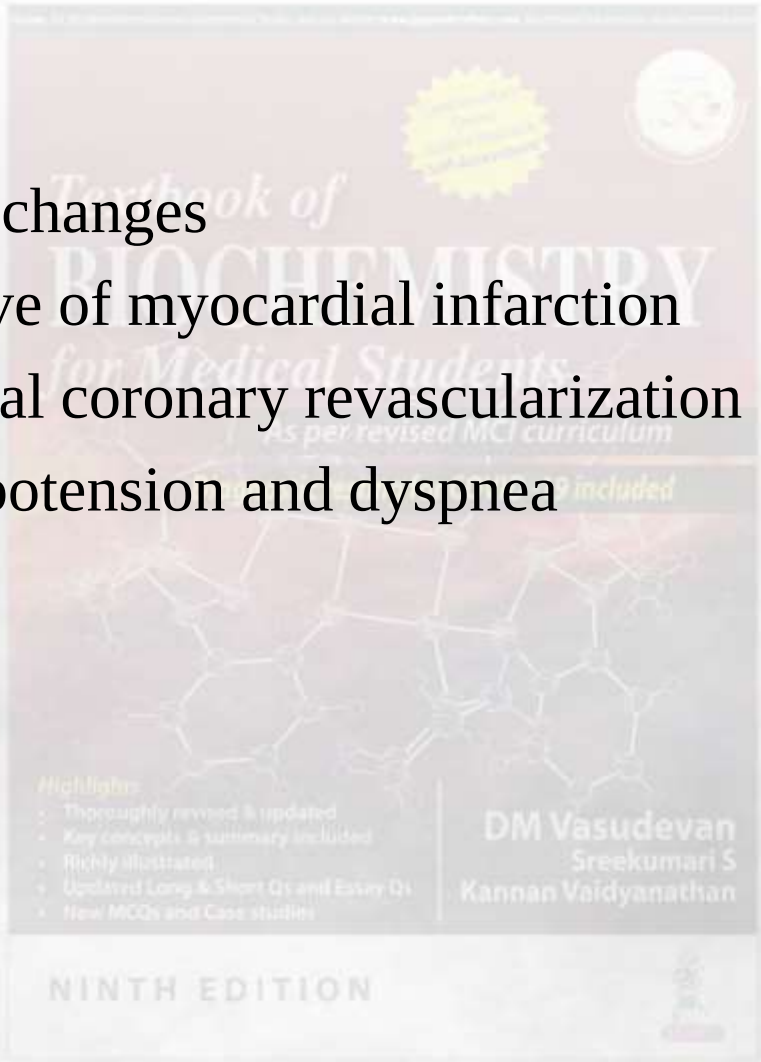
Cardiac markers may be classified as

1. Those for assessing acute cardiac injury. Commonly used biomarkers for early detection of acute myocardial infarction are cardiac troponins (cTnI and cTnT) and creatine kinase isoenzyme (CK-MB).
2. The risk factors (risk predictors) for atherosclerosis mainly include cholesterol, lipoproteins and hs-CRP in plasma.



Cardiac markers are tested in:

1. Any chest pain
2. Unstable angina
3. Suspicious ECG changes
4. History suggestive of myocardial infarction
5. Following surgical coronary revascularization
6. Patients with hypotension and dyspnea



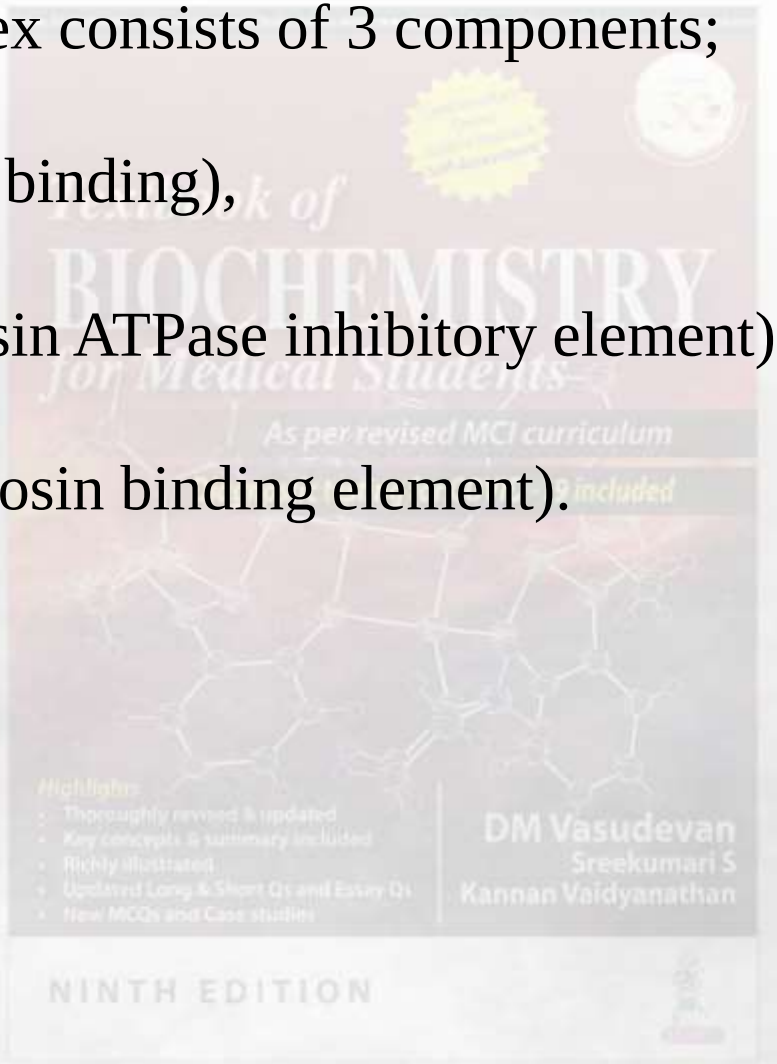
Cardiac Troponins (CTI/CTT)

The troponin complex consists of 3 components;

troponin C (calcium binding),

troponin I (actomyosin ATPase inhibitory element), and

troponin T (tropomyosin binding element).



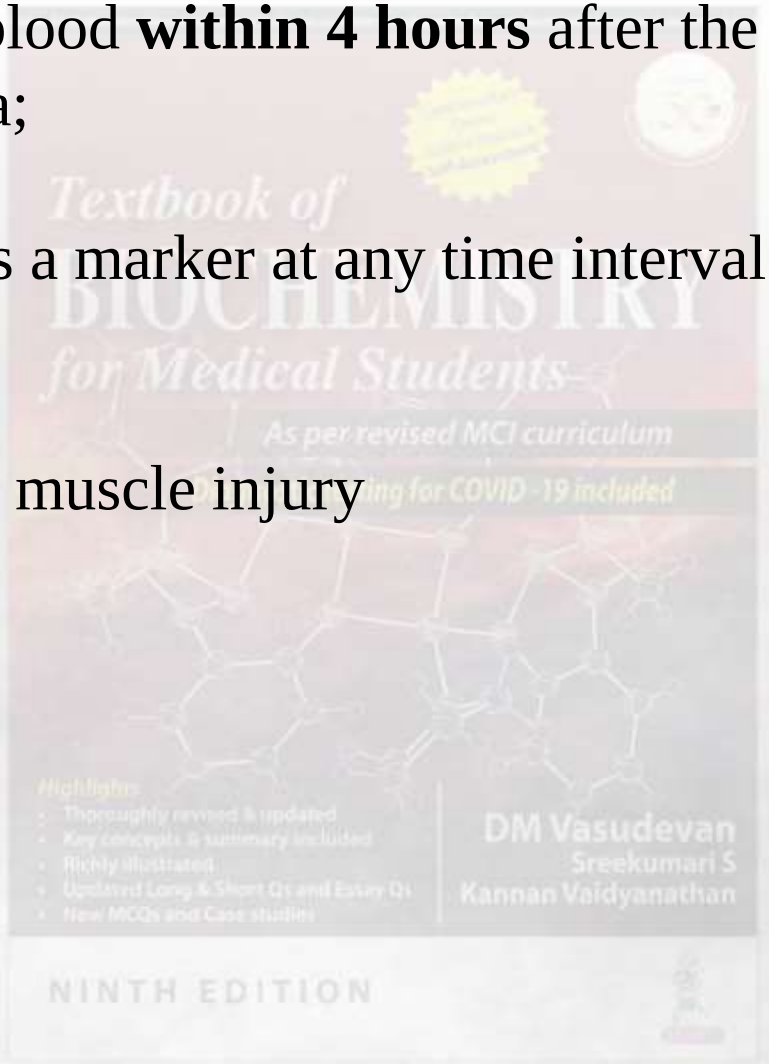
Troponin I

is released into the blood **within 4 hours** after the onset of myocardial ischemia;

CTI is very useful as a marker at any time interval after the heart attack.

It is not increased in muscle injury

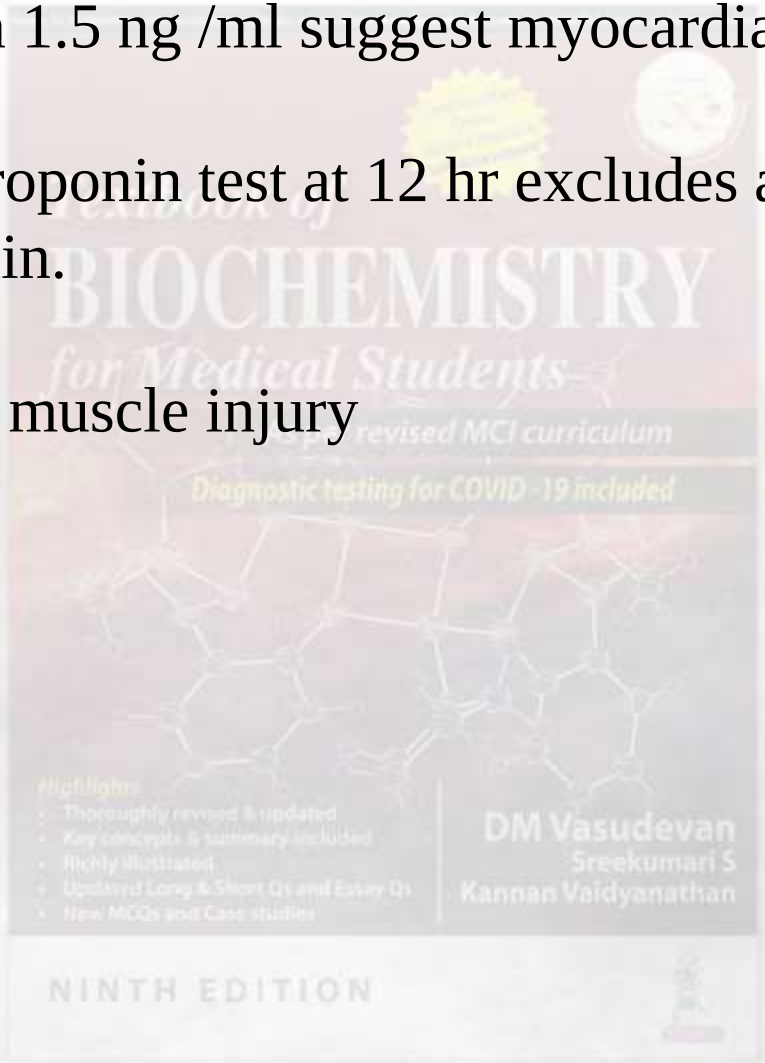
N value: 1 ng / ml



TnI levels more than 1.5 ng /ml suggest myocardial infarction.

A negative cardiac troponin test at 12 hr excludes an acute MI in a patient with chest pain.

It is not increased in muscle injury



Troponin T (TnT)

Increases **within 4 hrs** of myocardial infarction,

N value: <0.01 ug/ml
Myocardial infarction, >0.03 ug/ml.

The level of Troponin will generally reflect the infarct size.

Troponins are more sensitive than CK-MB to detect micro infarction.

- Serial estimations of cardiac troponins are done in any patient reporting with symptoms to the emergency clinic.
- Even without ECG changes, the present day protocol is to assay troponins, immediately on reaching the emergency room, then at 3 hours, 6 hours and 12 hours.
- An increasing blood value of troponin is the confirmation that patient has a myocardial infarction (MI).
- Troponin estimation could detect the MI, even before ECG changes are noticed.

High Sensitivity Cardiac Troponins (hs-cTnT or hs-cTnI)

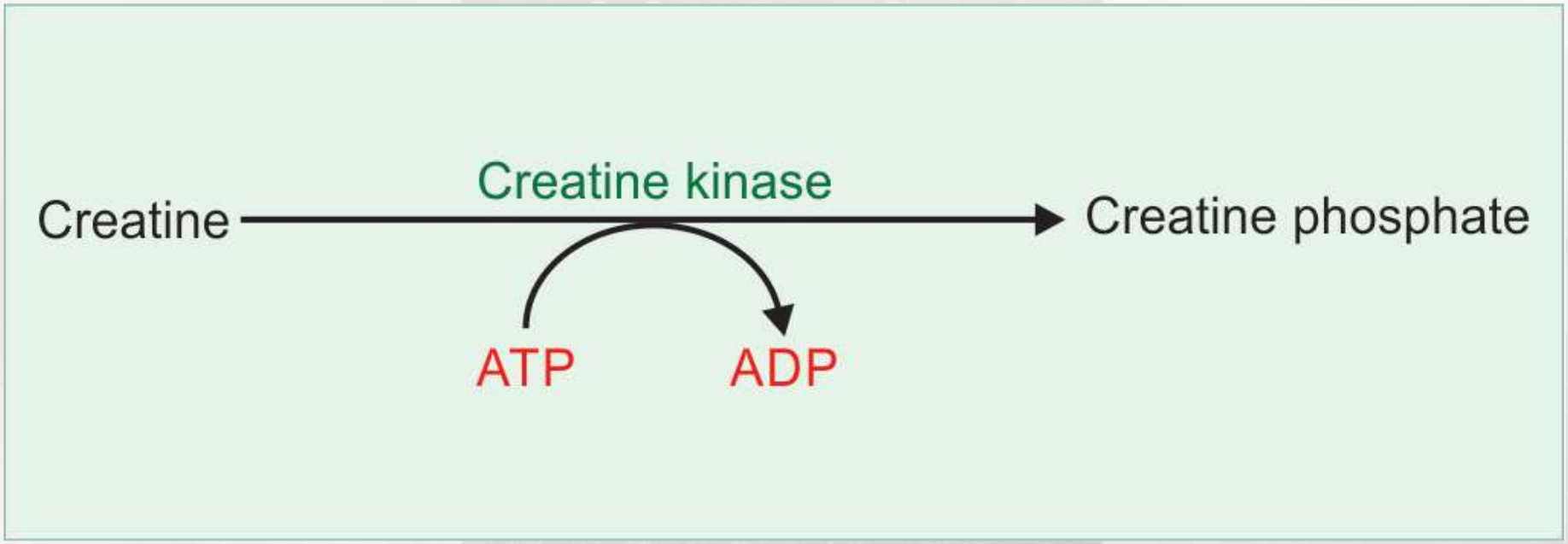
The higher sensitivity of this assay has allowed for improved identification of patients with AMI presenting in the first 3 hours following onset of symptoms. At least two measurements of high sensitive troponins are required for the assessment of patients with chest pain; the first measurement should be at presentation and the second sample should be measured 3 hours after. A rise of 20–100% is equivocal and needs further evaluation. Greater than 100% rise is consistent with myocardial infarction. The hs-cTnT values increase with increasing age especially at ages more than 60 years and also in patients with impaired renal function.

Creatine kinase (CK)

Normal Values

15–100 U/L for males and

10–80 U/L for females.

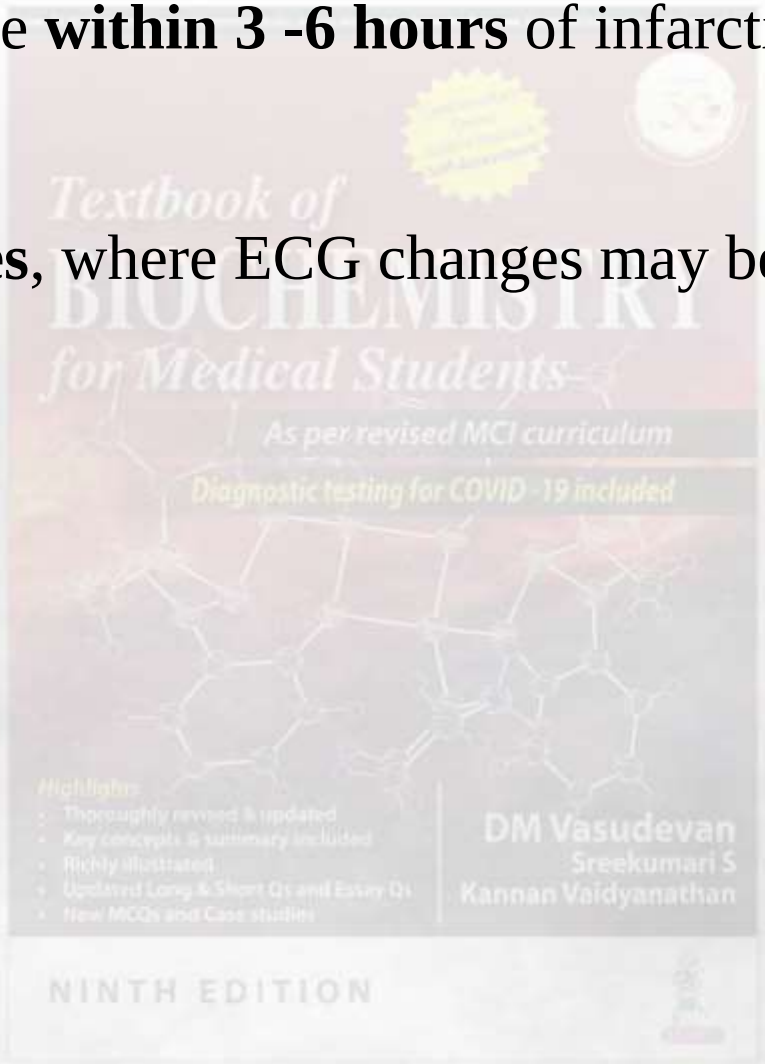


CK and Heart Attack

CK level starts to rise **within 3 -6 hours** of infarction.

Advantage

To **detect early cases**, where ECG changes may be ambiguous.



Characteristics of isoenzymes of CK

Iso-enzyme	Electro-phoretic mobility	Tissue of origin	Mean percentage in blood
CK-MM	Least	Skeletal muscle	80%
CK-MB	Inter-mediate	Heart	5%
CK-BB	Maximum	Brain	1%

CK and Muscle Diseases

The level of CK in serum is very much elevated in **muscular dystrophies** (500 -1500 IU/L)

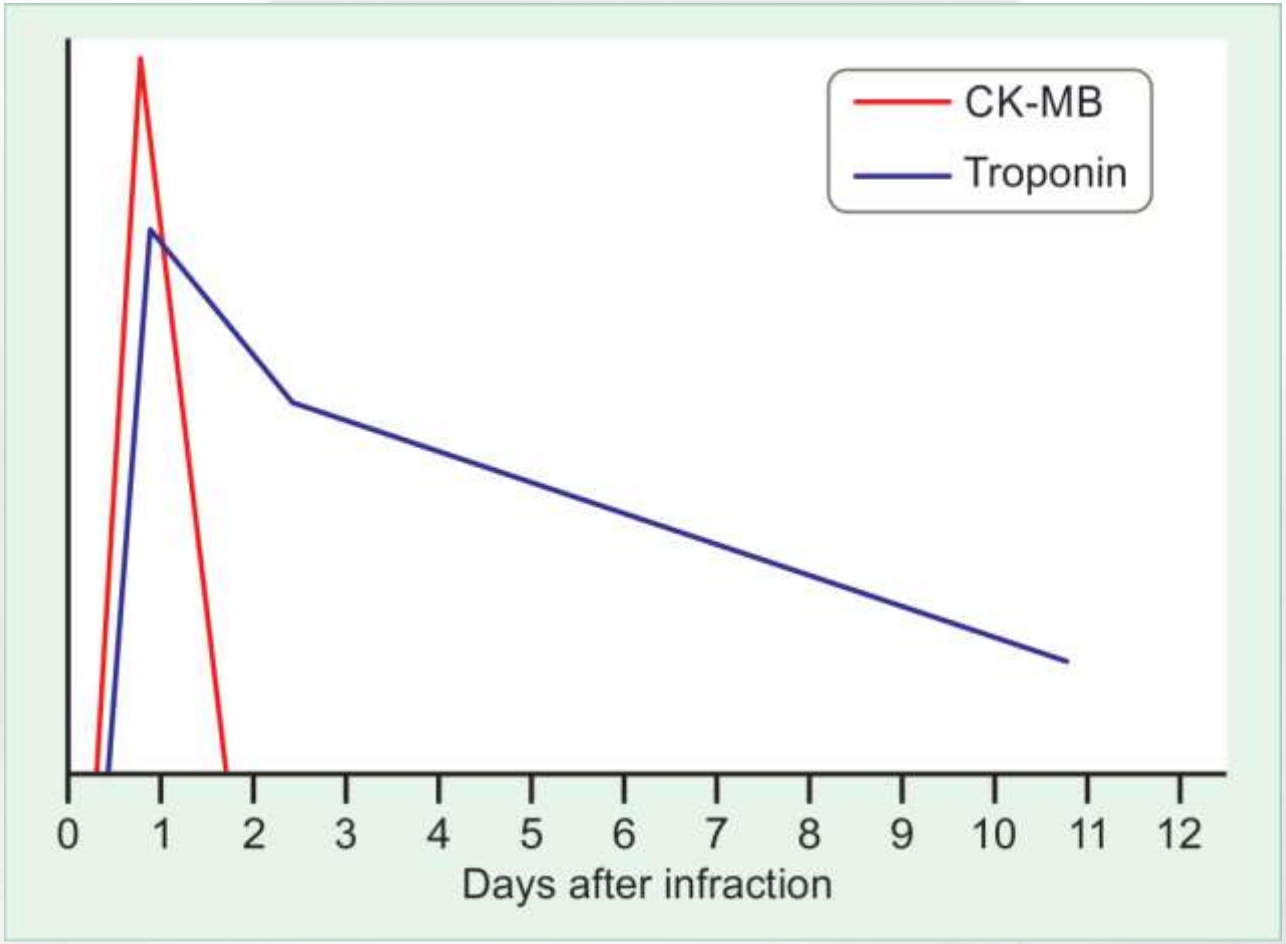
CK level is highly elevated in crush injury, fracture and acute cerebrovascular accidents.

Estimation of total CK is employed in muscular dystrophies and MB iso-enzyme is estimated in myocardial infarction.

Isoenzymes of Creatine Kinase

Creatine kinase is a dimer, the subunits are called B for brain and M for muscle. There are, therefore, three different isoenzymes: CK-MM, CK-BB and CK-MB. Skeletal muscle expresses CK-MM (98%) and low levels of CK-MB (1%).

Normally CK-MB (heart isoenzyme) is only 5% of the total activity. Even doubling of the value of CK-MB isoenzyme may not be detected, if total value of CK alone is estimated. Hence the estimation of **CK-MB isoenzyme** is important for the diagnosis of myocardial infarction.



Time course of elevation of cardiac troponins and CK-MB.

Myoglobin

It is raised after myocardial infarction; but is not specific as it is raised during muscle injuries. It has the advantage of responding very rapidly, rising and falling earlier than CKMB or troponin.

Myoglobin is released as early as 1–2 hours after onset of symptoms during AMI. It is highly sensitive for AMI detection within the first few hours after presentation. In contrast, cTn assays increase 3–6 hours after symptom onset in AMI.

A **negative value** of myoglobin will exclude infarction and is useful in the early hours of chest pain.

Lactate Dehydrogenase

LDH, especially the cardiac variety was used extensively as a myocardial disease marker in olden days.

As it is increased in blood only after 6–12 hours after the onset, it is not useful for early detection. Moreover, LDH is highly nonspecific, as the level is increased in various other diseases.

Hence it is rarely used nowadays.

Brain Natriuretic Peptide

Atrial natriuretic peptide (ANP) and brain natriuretic peptide (BNP) are used in cardiology. ANP is produced primarily in the cardiac atria. BNP is present in human brain, but more in the cardiac ventricles. Patients with **congestive heart failure** have high plasma concentrations of ANP and BNP. The concentrations are correlated with the extent of ventricular dysfunction. High concentrations of BNP predict poor long-term survival. BNP test helps to differentiate heart failure or obstructive lung disease as the cause for breathlessness. Patients with chronic obstructive pulmonary disease (COPD) and worsening of their cor pulmonale with signs of right ventricle volume overload (including edema and ascites) manifest increased BNP levels.

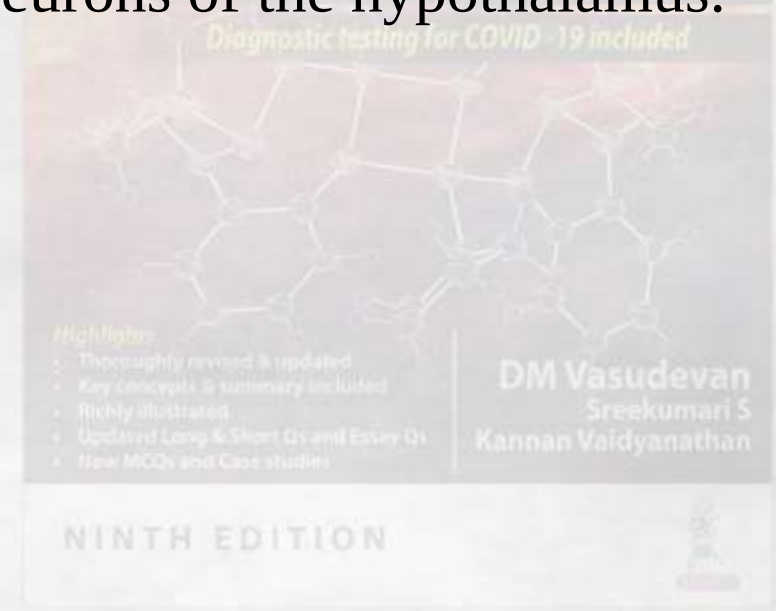
Markers of Myocardial Infarction

Marker	Onset	Peak	Dura-tion	Remarks
Troponins	4-10 hr	18-24hr	8-14 d	Preferred marker
CK-MB	3-6 hr	18-24hr	36-48hr	Useful marker
Myoglobin	1-4 hr	6-7 hr	24 hr	Nonspecific
LDH	6-12 hr	24-48hr	6-8 d	Not used nowadays

Candidate Markers for Myocardial Infarction

The following few parameters are still in experimental or clinical trial stages and are not yet routinely done in clinical laboratories.

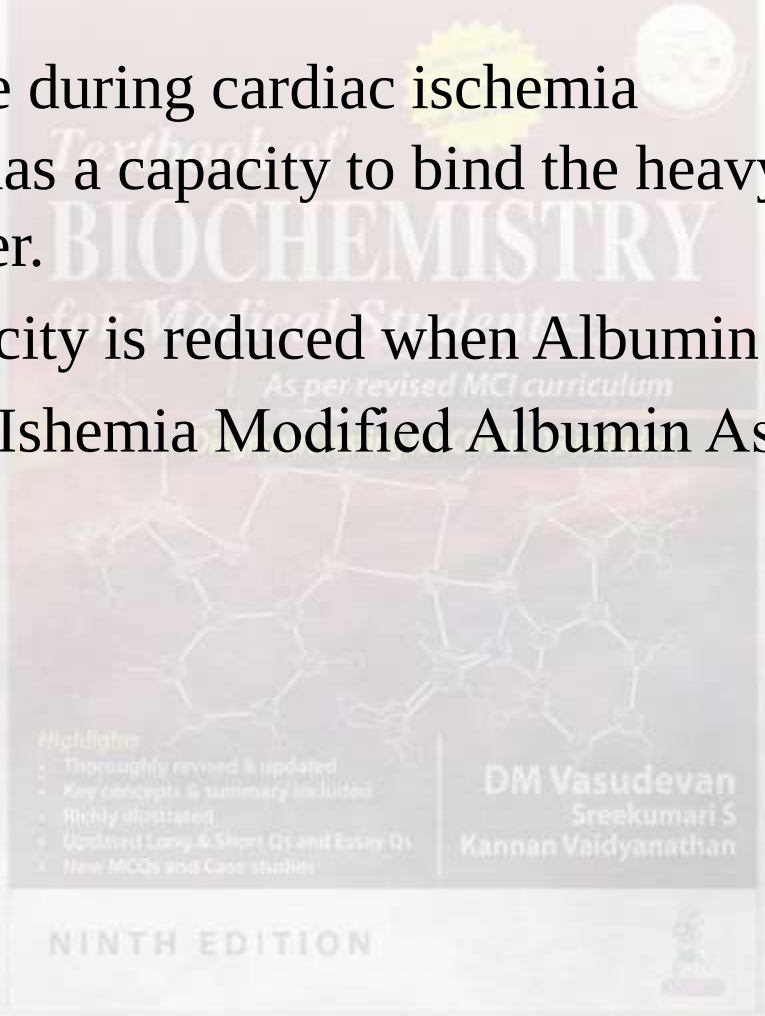
1. **Ischemia modified albumin** (IMA)
2. **Adrenomedullin** (**AM**) is a vasodilator peptide.
3. **Copeptin** (also known as CT-proAVP) is synthesized in the paraventricular neurons of the hypothalamus.



Ischemia Modified Albumin

A major breakthrough in cardiac testing

- Oxidative damage during cardiac ischemia
- Serum Albumin has a capacity to bind the heavy metal ions like Cobalt and Copper.
- The binding capacity is reduced when Albumin is damaged.
- the test is called ‘Ishemia Modified Albumin Assay’.



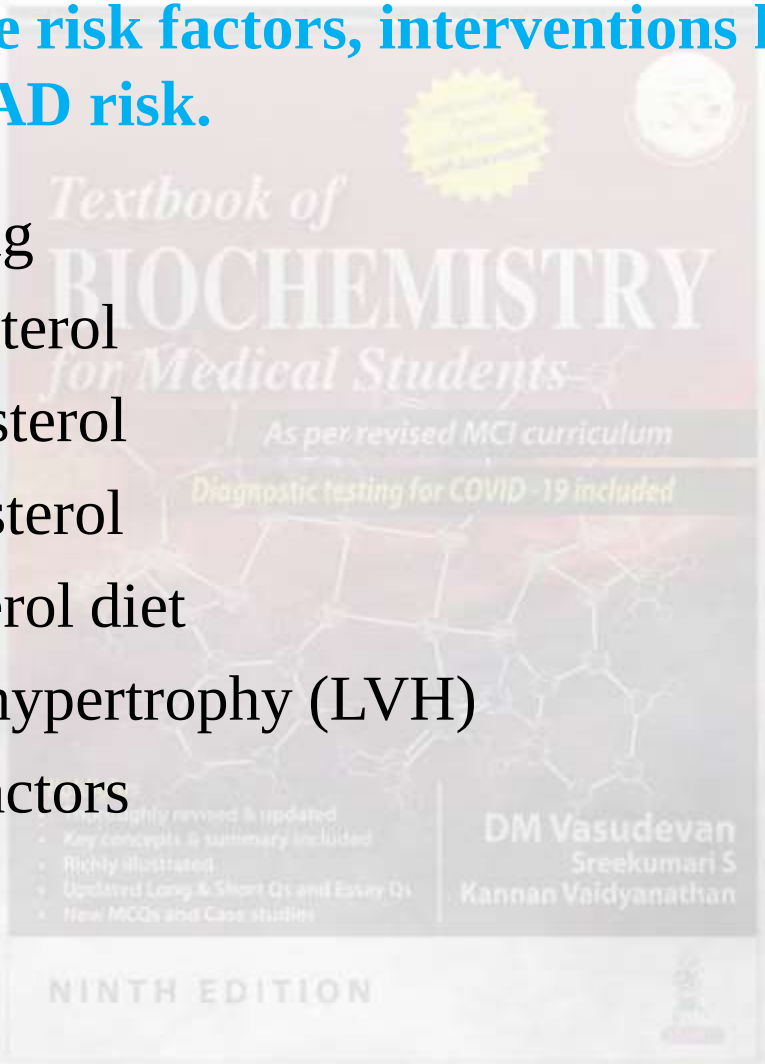
Ischemia Modified Albumin

- IMA test is very easy to perform
- It can serve as a 'Point-of-care' test in cardiac ICU
- Shows a very good correlation with the other cardiac markers
- Cost Effective
- A High Predictive Value of a negative IMA test is highly useful, where it can guide to shift the patient out of ICU thus saving precious resources.

Risk factors for Atherosclerosis and cardiac diseases

Class 1: Modifiable risk factors, interventions have been proved to lower CAD risk.

1. Cigarette smoking
2. High total cholesterol
3. High LDL cholesterol
4. Low HDL cholesterol
5. High fat/cholesterol diet
6. Left ventricular hypertrophy (LVH)
7. Thrombogenic factors



Risk factors for Atherosclerosis, continued

Class 2: Modifiable risk factors, interventions are likely to lower CAD risk.

1. Lipoprotein (a) or Lp(a)
2. Diabetes mellitus
3. Hypertension
4. Physical inactivity
5. Obesity
6. High serum triglyceride
7. High serum homocysteine
8. Increased high-sensitivity-CRP (hs-CRP)
9. Stress

Class 3: Nonmodifiable risk factors.

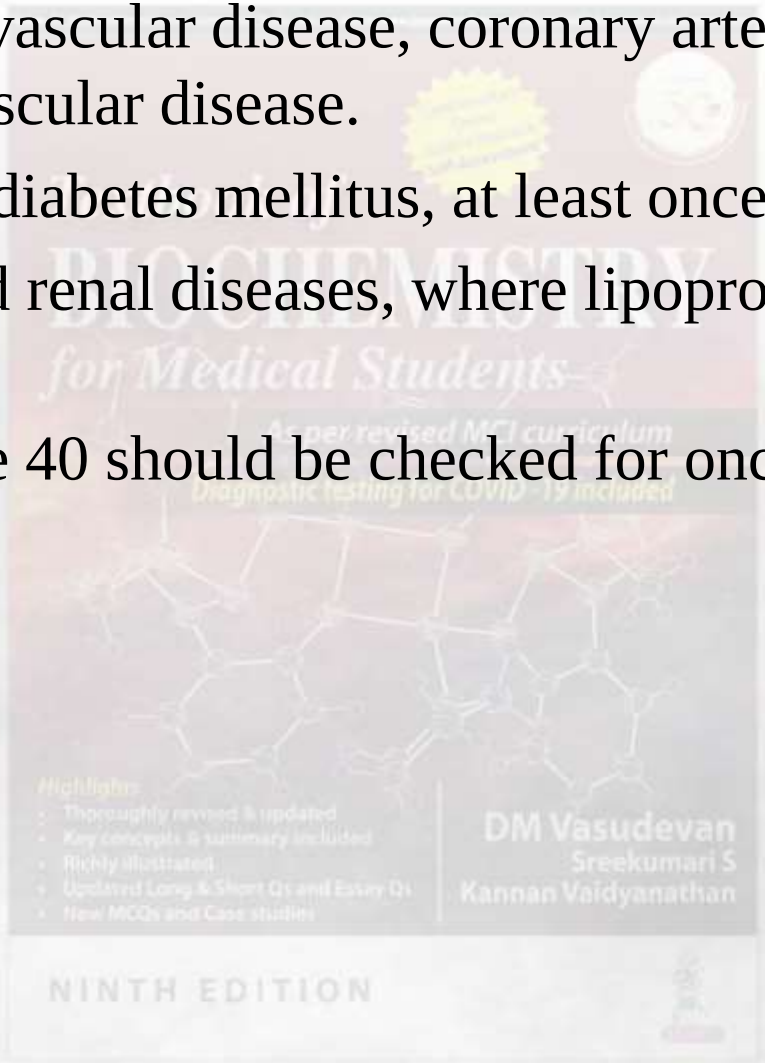
1. Age
2. Male gender
3. Family history of CAD

Serum Cholesterol level is increased in

1. **Diabetes mellitus:** Acetyl CoA pool is increased and more molecules are channelled to cholesterol.
2. **Obstructive jaundice:** The excretion of cholesterol through bile is blocked.
3. **Hypothyroidism:** The receptors for HDL on liver cells are decreased, and so excretion is not effective.
4. **Nephrotic syndrome:** Albumin is lost through urine, globulins are increased as a compensatory mechanism. So, apolipoproteins are increased, and then cholesterol is correspondingly increased.
5. **Familial hyper lipoproteinemias**

When should we check lipid profile?

1. Suspected cardiovascular disease, coronary artery disease and peripheral vascular disease.
2. All patients with diabetes mellitus, at least once in 6 months.
3. Thyroid, liver and renal diseases, where lipoprotein metabolism may be altered.
4. All persons above 40 should be checked for once in a year.



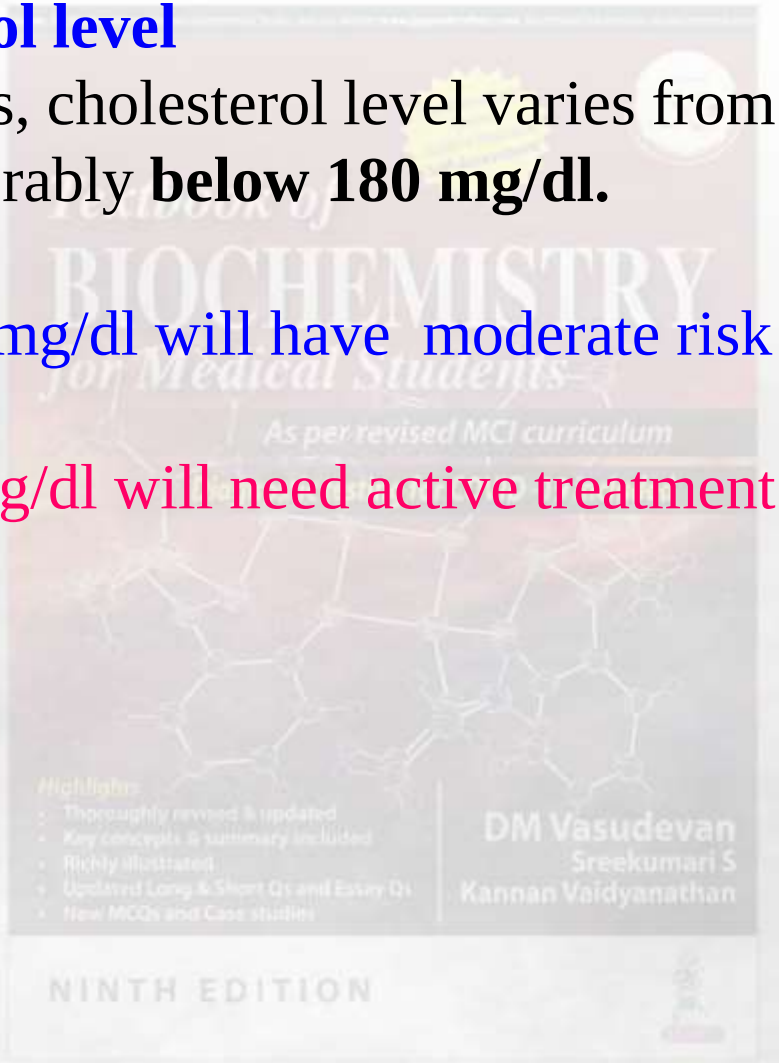
Risk Factors for Atherosclerosis

1. Serum cholesterol level

In normal persons, cholesterol level varies from 150 to 200 mg/dl. It should be preferably **below 180 mg/dl.**

Values around 220 mg/dl will have moderate risk

Values above 240 mg/dl will need active treatment.



2. LDL-cholesterol level

Blood levels **under 130 mg/dl** are desirable.

Levels between 130 and 159 are borderline;
while above 160 mg/dl carry definite risk.
Hence LDL is **"bad"** cholesterol.

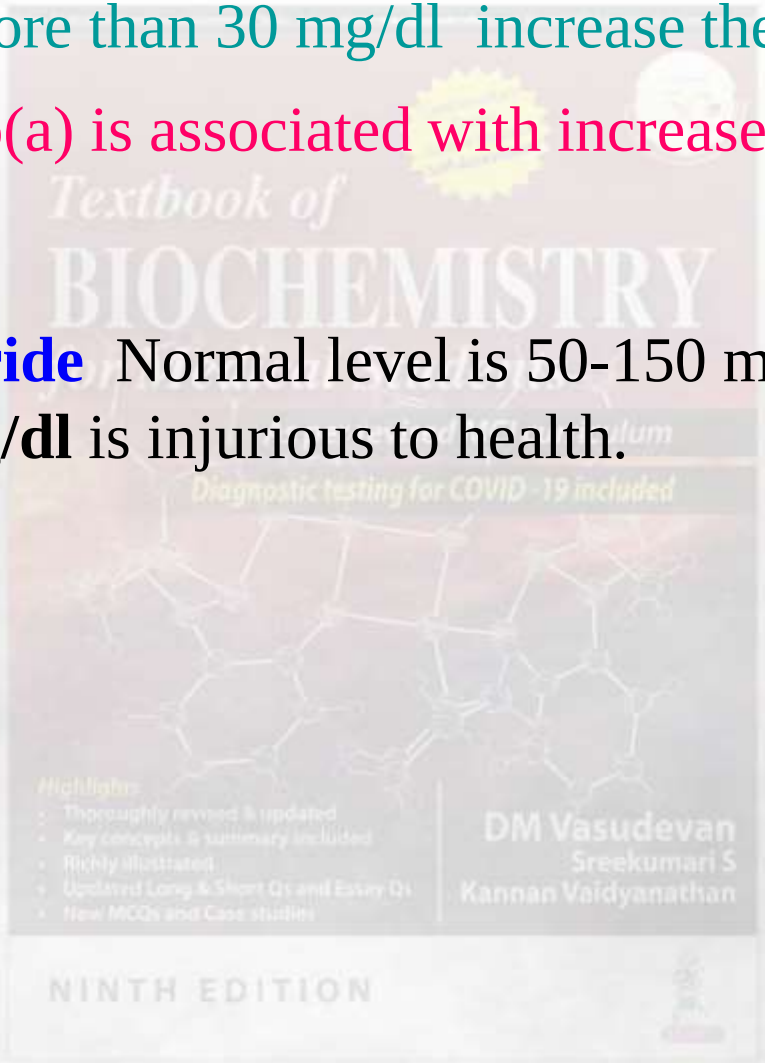
3. HDL-cholesterol level

- HDL level **above 60 mg/dl** protects against heart disease.
- Below 40 mg/dl increases the risk.
- Hence HDL is "good" cholesterol.

4. Lp(a) Levels more than 30 mg/dl increase the risk 3 times.

When increased Lp(a) is associated with increased LDL, the risk is increased 6 times.

5. Serum triglyceride Normal level is 50-150 mg/dl. Blood level **more than 150 mg/dl** is injurious to health.



Non-HDL cholesterol and evaluation of cardiovascular risk

Non-HDL cholesterol or atherogenic cholesterol = LDL+ VLDL+ IDL+ Lp(a).

As per NCEP guidelines, the value of non-HDL-C is important for the risk evaluation.

100–130 mg/dL = Very little risk

130–160 mg/dL = Borderline risk

160–190 mg/dL = High-risk

>190 mg/dL = Very high-risk

Cardiovascular disease risk and lipid parameters

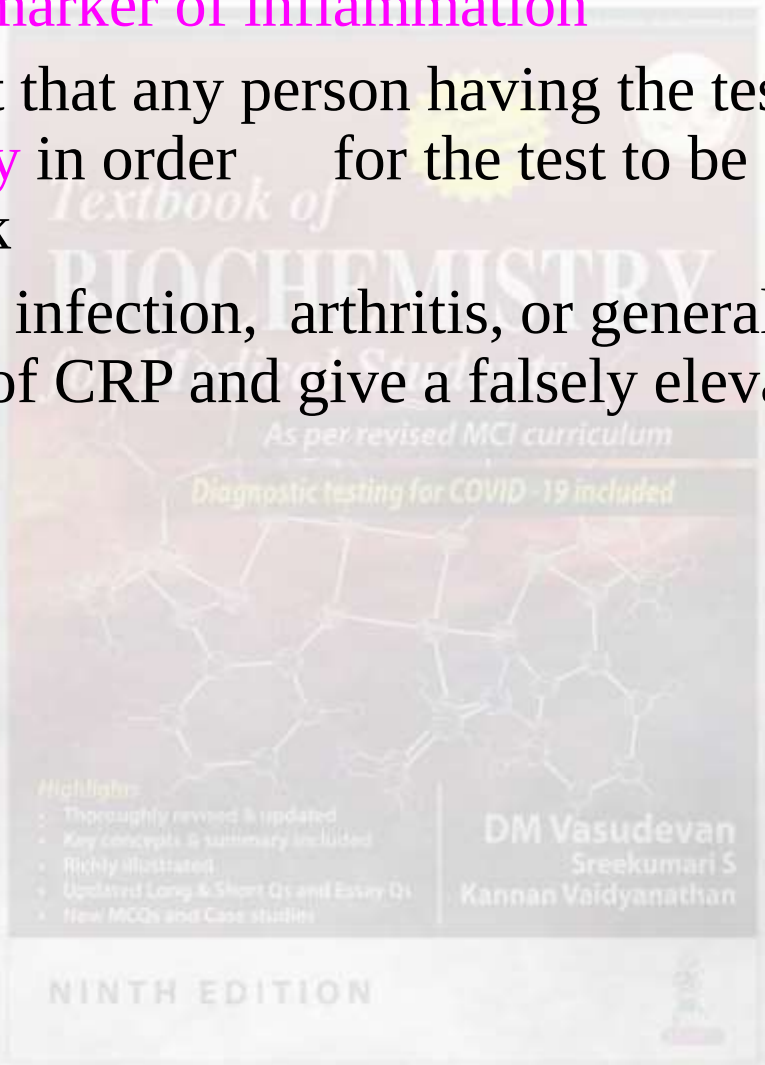
	Low risk (desirable level)	Borderline risk	High risk
Total cholesterol (mg/dL)	< 200	200-240	>240
LDL cholesterol (mg/dL)	<130	130-160	>160
HDL cholesterol (mg/dL)	>60	35-60	<35
Triglyceride (mg/dL)	<150	200-400	>400

High sensitivity CRP (hs-CRP)

- To predict a healthy person's risk of cardiovascular disease.
- High hs-CRP values have 1.5 to 4 times the risk of having a heart attack
  - Low risk: less than 1.0 mg/L
  - Average risk: 1.0 to 3.0 mg/L
  - High risk: above 3.0 mg/L
- Atherosclerosis is also an inflammatory process; but low level of long-term inflammation produces only small amounts of CRP.
- Therefore, the test requires higher sensitivity than previous tests.
- Thus, this test is known as high-sensitivity CRP or hs-CRP.

High sensitivity CRP (hs-CRP)

- The hs-CRP is a marker of inflammation
- So, it is important that any person having the test be apparently healthy in order for the test to be of any value in predicting the risk
- Any tissue injury, infection, arthritis, or general inflammation will raise the amount of CRP and give a falsely elevated estimate of risk.



Homocysteine level

Plasma homocysteine above 15 micromol / L will increase the risk of coronary artery disease and stroke at a **younger age**.

Administration of pyridoxine, vitamin B12 and folic acid may lower the homocysteine level.

Obesity and Sedentary life style

The classical description of Pickwick by Charles Dickens reminds of a person with high risk for CAD.

Lipoprotein-associated Phospholipase A2 (LpPLA2)

It is also known as platelet-activating factor acetylhydrolase (PAF-AH). It is an enzyme produced by inflammatory cells. It is expressed in the diseased vessel and considered to be a marker for plaque instability. Unlike hs-CRP, the LpPLA2 test is not affected by conditions other than CVD. So, when there is general inflammation, such as arthritis, LpPLA2 test may be used. LpPLA2 is a relatively new test and its clinical usefulness has yet to be established. The test is not diagnostic of CHD or ischemic stroke; it is a risk indicator.

Prevention of Atherosclerosis

1. **Moderation in dietary fat and cholesterol**
2. **Vegetable oils and PUFA**
3. **Green leafy vegetables**
4. **Avoid sucrose**
5. **Avoid cigarette**
6. **Do exercise**

Regular moderate exercise will lower LDL (bad cholesterol) and raise HDL (good cholesterol) levels in blood. It will also reduce obesity.

7. **Hypolipidemic drugs**

Dietary Therapy

Total Calories- To achieve and maintain desirable weight

Total Carbohydrate - >55% of total calories

Protein - 15% of total calories

Total fat - < 30% of total calories

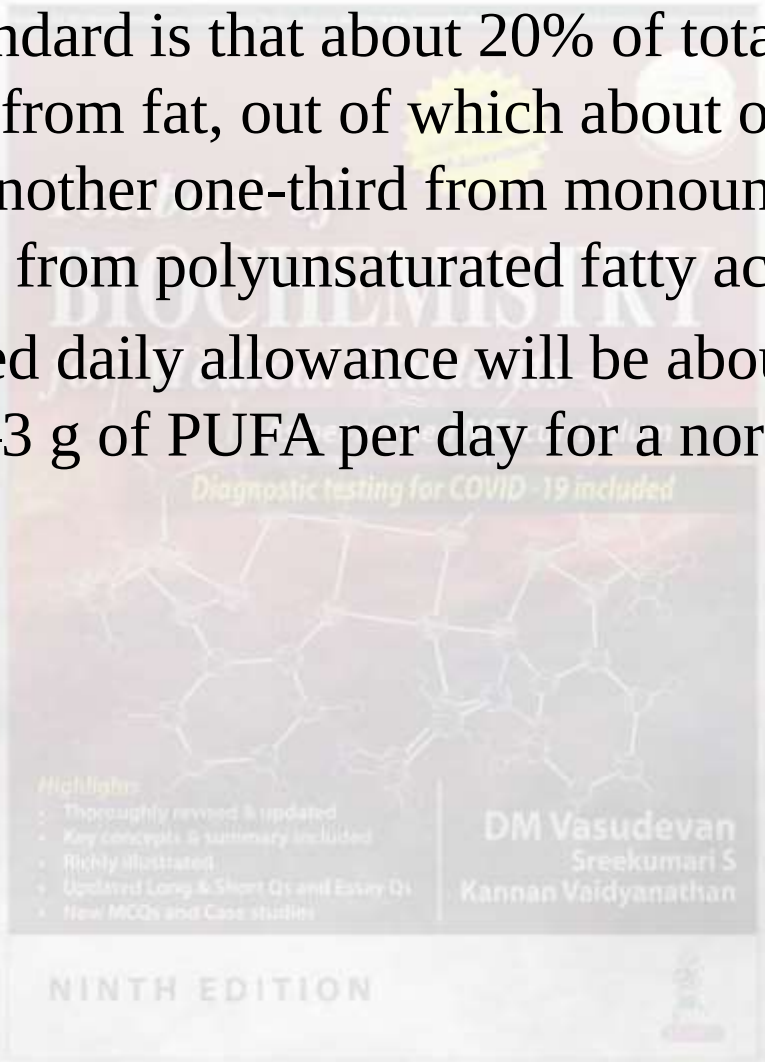
Saturated fatty acids - < 10% of total calories

Vegetable Oils and PUFA

- Vegetable oils (e.g. sunflower oil) and fish oils contain polyunsaturated fatty acids (PUFA).
- They are required for the esterification and final excretion of cholesterol.
- So PUFA is helpful to reduce cholesterol level in blood.
- **Omega-3 fatty acids** from fish oils reduce LDL and decrease the risk of CAD.
- Recommended intake of omega-3 fatty acid (fish oils) is 1 g/day (EPA and DHA combined).
- Clinical studies have suggested that DHA, (docosahexenoic acid) and EPA, (eicosapentaenoic acid) lower triglycerides; slow the buildup of atherosclerotic plaques; as well as reduce the risk of heart attack.

Moderation in Fat Intake

- The accepted standard is that about 20% of total calories may be obtained from fat, out of which about one-third from saturated, another one-third from monounsaturated and the rest one-third from polyunsaturated fatty acids.
- The recommended daily allowance will be about **20–25 g of oils** and about 2–3 g of PUFA per day for a normal adult.



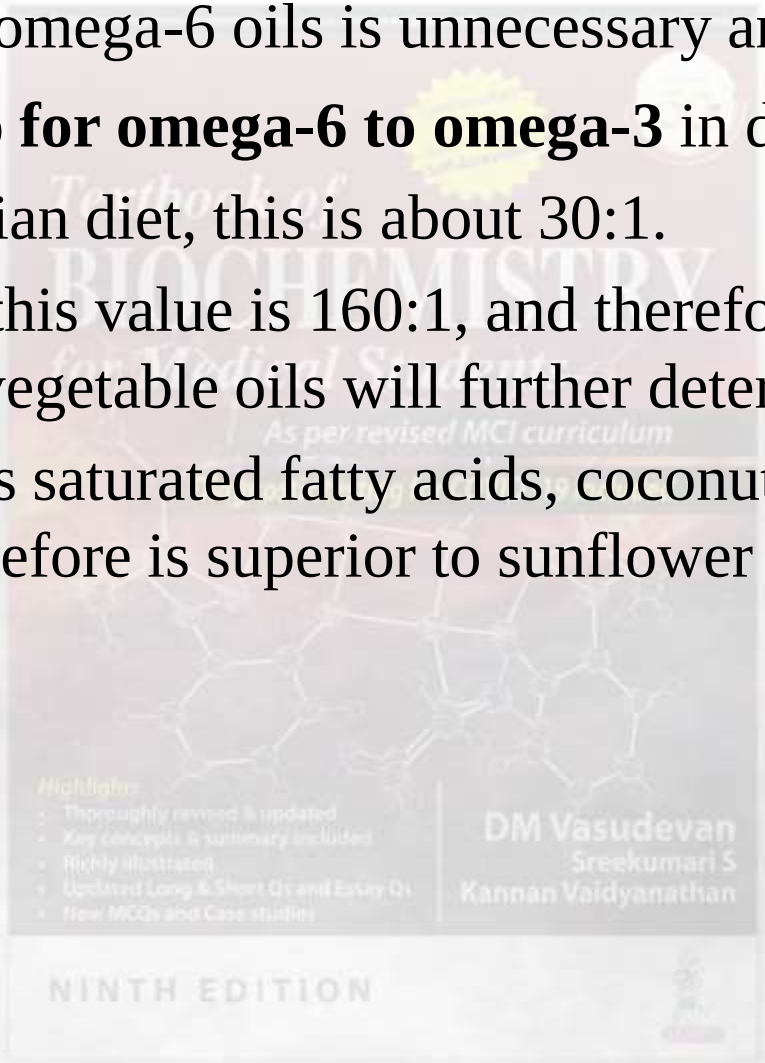
Avoid Trans Fatty Acids (TFA)

- Trans fatty acids (with double bonds having trans configuration) are formed during the partial hydrogenation of vegetable oils.
- They are widely used in food industry because of their long shelf-life.
- Trans fatty acids (TFA) are found to be more atherogenic than saturated fatty acids.
- It alters secretion and composition of apo-B100 containing lipoproteins (LDL and VLDL).
- It increases catabolism of apo-A-I, decreases HDL and increases LDL levels.
- Reducing the intake of TFA to 2–7 g/day is now strongly advised.

PUFA, in Excess, may be Harmful

- PUFA can definitely reduce cholesterol level.
- But there should be moderation.
- It is known that the diet should contain correct type and quantity; the optimum ratio of omega-6 to omega-3 fatty acids is 4:1.
- Very high intake of omega-6 oils will cause lowering of HDL, elevation of plasma triglycerides, and will promote platelet aggregation.
- Vegetable oils (sunflower oil) containing PUFA are rich in omega-6 variety; while ghee and butter are low in omega-6.
- Omega-3 group is present in fish oils.
- Normal Indian diet consisting of cereals, pulses and vegetables provides **"invisible oils"**, which contains about 10 g of PUFA/ day (out of which about 2 g is omega-3 and the rest 8 g is omega-6).

- Further intake of omega-6 oils is unnecessary and may be harmful.
- The optimal **ratio for omega-6 to omega-3** in diet is 4:1.
- In an average Indian diet, this is about 30:1.
- In sunflower oil, this value is 160:1, and therefore, unnecessary addition of such vegetable oils will further deteriorate the condition.
- Although contains saturated fatty acids, coconut oil has the omega ratio 3:1, and therefore is superior to sunflower oil in this respect.



Green Leafy Vegetables

- Due to their **high fiber content,** leafy vegetables will increase the motility of bowels and reduce reabsorption of bile salts.
- Vegetables also contain plant sterols (**sitosterol**) which decrease the absorption of cholesterol.
- About 400 g/day of fruit and vegetables are desirable.

When to start Statins?

1. All patients with established cardiovascular disease (secondary prevention).
2. Patients with diabetes mellitus, over 40 years of age.
3. Diabetes mellitus with other risk factors such as retinopathy, nephropathy, microalbuminuria, hypertension.
4. Total cholesterol above 220 mg/dL or LDL more than 160 mg/dL or total cholesterol: HDL ratio more than 6.
5. Family history of premature CVD.
6. Lifestyle alterations (exercise and diet) are not enough to reduce the cholesterol level.

Plant derived products having cholesterol lowering action

Plant derived fiber: Reduces serum cholesterol

Legumes: Reduces cholesterol even on high fat diet

Onion and garlic: Reduce serum cholesterol and TG

Embelia ribes (vidanga): Dried berries alone or along with amla has hypolipidemic effect

Commiphora mukul (guggulu): Hypolipidic and cardioprotective

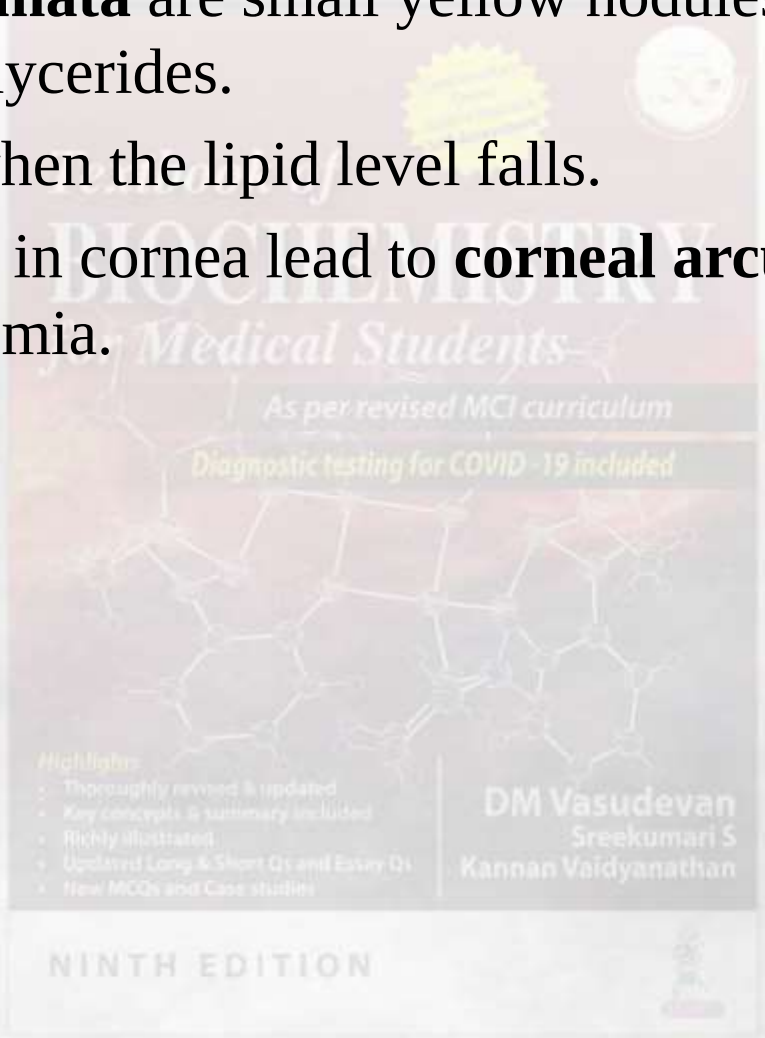
Cyperus rotundus (musta): Hypolipidemic; improves metabolic activity

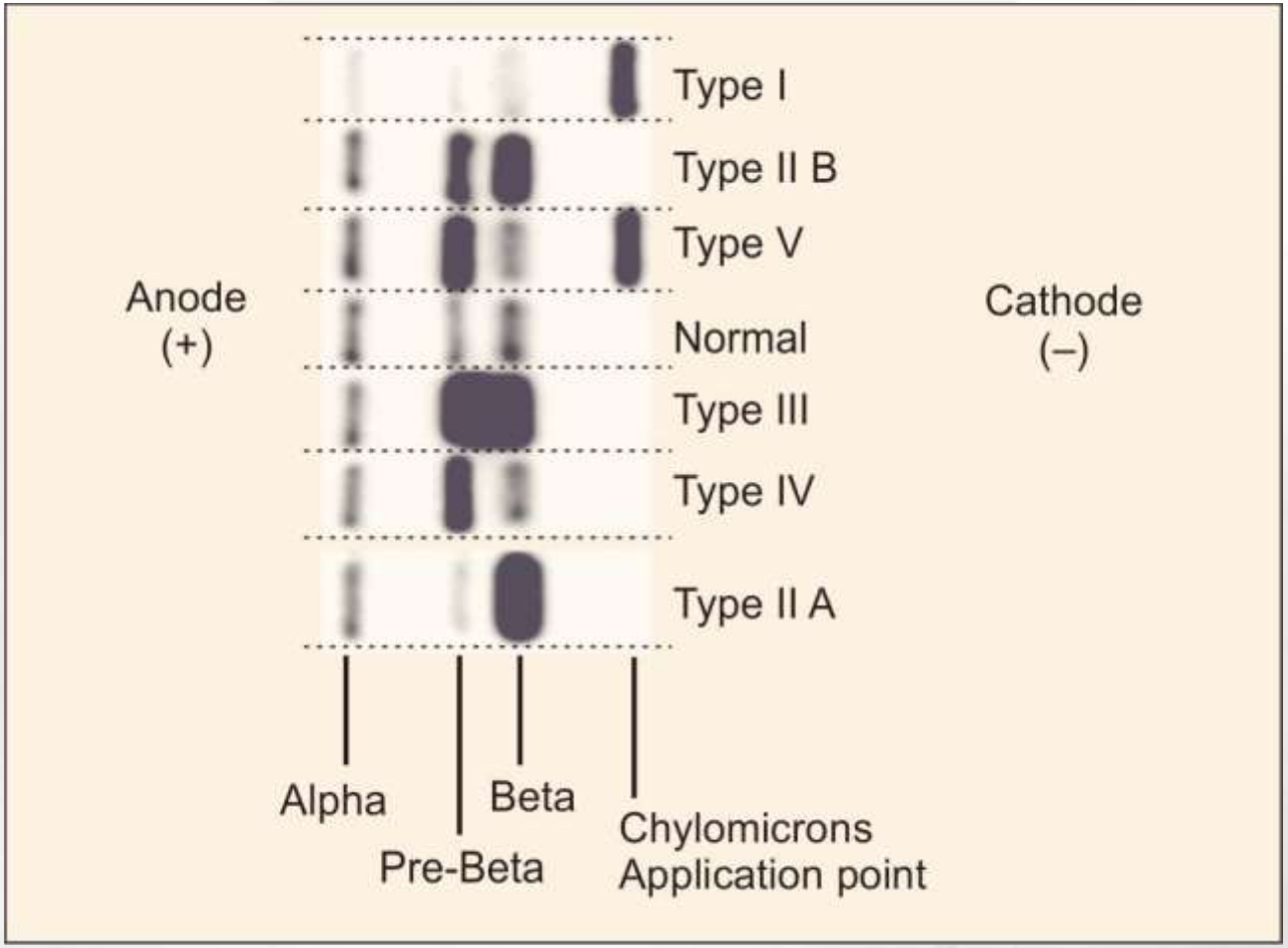
Spices, flavinoids: Natural antioxidants prevent oxidative modification of LDL

Hyperlipidemias

- **Fredrickson's** classification is the most widely accepted.
- In all cases of hyperlipidemias, the elevated lipid fraction is either cholesterol or TAG or both.
- The elevation of lipids in plasma leads to the deposition of cholesterol on the arterial walls, leading to **atherosclerosis.**
- The coronary and cerebral vessels are more commonly affected.
- Thromboembolic episodes in these vessels lead to **ischemic heart disease** and cerebrovascular accidents.
- The deposition of lipids in subcutaneous tissue leads to **xanthomas**.
- The type of xanthoma depends on the nature of lipid deposited.

- **Eruptive xanthomata** are small yellow nodules associated with deposition of triglycerides.
- They disappear when the lipid level falls.
- Deposits of lipids in cornea lead to **corneal arcus**; indicating hypercholesterolemia.





Electrophoretic pattern of hyperlipidemias

BOX 15.8: Clinical classification of hyperlipidemias (for treatment purpose)

Classification	*Type*	*Salient features*
Hypercholesterolemia	Type IIa	Increased LDL
Hypertriglyceridemia	Type I, Type IV and Type V	Increased VLDL
Increased chylomicrons,		
Combined hyperlipidemia	Type IIb and Type III	Increased VLDL, Increased IDL

Type IIA (Primary Familial Hypercholesterolemia)

- Patients seldom survive the second decade of life due to ischemic heart disease.
- There is elevation of LDL. The cause is **LDL receptor** defect.
- Receptor deficiency in liver and peripheral tissues will result in the elevation of LDL levels in plasma, leading to hypercholesterolemia.
- The LDL receptor defect may be due to the following reasons.
  1. **LDL receptor deficiency.**
  2. **Defective binding** of B-100 to the LDL receptors. This defect is known as B-3500 or **familial defective apo B.**
  3. Receptor-LDL complex is not internalized.
- Secondary type II hyperlipoproteinemia is seen in hypothyroidism, diabetes mellitus, nephrotic syndrome and cholestasis.

TABLE 15.4: Fredrickson's classification of hyperlipoproteinemias (N = Normal; ↑ = Increased)

Type	*Lipoprotein fraction elevated*	*Cholesterol level*	*TAG level*	*Appearance of plasma after 24 hr*	*Metabolic defect*	*Features*	*Management*
Type I	Chylomicrons	N	↑↑	Creamy layer over clear plasma	Lipoprotein lipase deficiency	Eruptive xanthoma; hepatomegaly; Pain abdomen.	Restriction of fat intake. Supplementation with medium chain triglycerides
Type IIA	LDL	↑↑	N	Clear	LDL Receptor defect; Apo-B ↑	Atherosclerosis, coronary artery disease, Tuberous xanthoma	Low cholesterol diet. Decreased intake of saturated fat. Give PUFA and drugs like statins.
Type IIB	LDL and VLDL	↑↑	↑	Slightly cloudy	Apo-B ↑ Apo-CII	Corneal arcus	Do
Type III	Broad beta-VLDL and Chylomicrons	↑↑	↑	Cloudy	Abnormal apo-E; Apo-CII ↑	Palmar xanthoma. High incidence of vascular disease	Reduction of weight, restriction of fat and chol. Give PUFA and drugs
Type IV	VLDL	↑	↑↑	Cloudy or milky	Over-production of VLDL; Apo-CII ↑	Associated with diabetes, heart disease, obesity.	Reduction of body weight. Restrict carbohydrate and cholesterol
Type V	VLDL Chylomicrons	N	↑↑	Creamy layer over milky plasma	Secondary to other causes	Chronic pancreatitis	High PUFA intake, hypocholipidemic drug

TABLE 15.5: Secondary hyperlipidemias

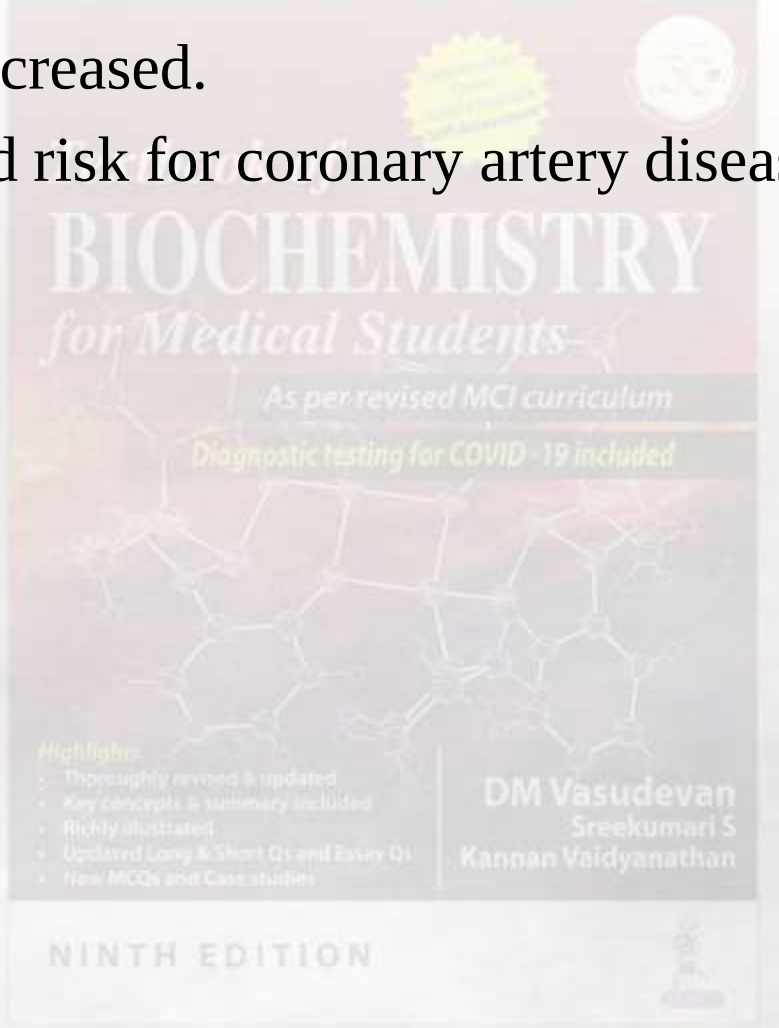
	Serum cholesterol	*Serum triglyceride*
Diabetes	Increased	Increased
Nephrotic syndrome	Increased	Increased
Hypothyroidism	Increased	Increased
Biliary obstruction	Increased	Normal
Pregnancy	Normal	Increased
Alcoholism	Normal	Increased
Oral contraceptives	Normal	Increased

Hypolipoproteinemias

- **Abetalipoproteinemia**
- All apo-B containing lipoproteins are reduced since microsomal triglyceride transfer protein is defective.
- Hence TAG is not incorporated into VLDL and chylomicrons.
- Beta lipoprotein (LDL) is absent.
- Fat-soluble vitamins are not absorbed, causing mental and physical retardation.
- Serum levels of triglycerides, cholesterol and phospholipids are extremely low.
- Blindness may occur as a result of degenerative changes in retina.
- Erythrocytes have spiny projections (**acanthocytes**).

Hypoalphalipoproteinemia

- This is inherited as an autosomal dominant trait.
- Serum HDL is decreased.
- There is increased risk for coronary artery diseases.



Tangier Disease

- It is a relatively benign, autosomal dominant condition.
- It is characterized by a defect in the efflux (flowing out) of cholesterol from cells, and reduction of HDL levels in the blood.
- The biochemical defect is the absence of **"ATP-Binding Cassette Transporter-1"** (ABC-1), which is involved in transferring cellular cholesterol to HDL.
- So, plasma HDL is low and alpha band is not seen in electrophoresis.
- Cholesterol esters are accumulated in tissues.
- Manifestations are large orange yellow tonsils, muscle atrophy, recurrent peripheral neuropathies and atherosclerosis.