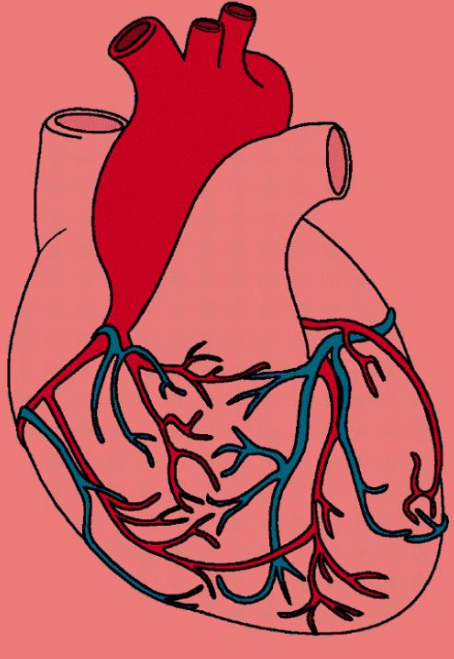
Editing File

SAQs Revision



- This file for **revision** and some possible SAQs.
- Beware the this file **only for revision** , you should study all the lectures.

changes in bicarbonate conc. In the extracellular fluid.

Lactic Acidosis

Q: What are the types of metabolic acid-base disorders:

1. Metabolic acidosis.
2. Metabolic alkalosis.

Q: Metabolic acidosis can occur due to?

1. Increased production of H+ ions.
2. Ingestion of H+ or drugs metabolized to acids.
3. Impaired excretion of H+.
4. Loss of bicarbonate ions e.g Chronic diarrhea and Renal tubular Acidosis .

Q: Metabolic alkalosis can occur due to?

1. Loss of H+ ions in gastric fluid due to vomiting.
2. Ingestion of sodium bicarbonate.
3. Potassium deficiency as a result of diuretic therapy.

Q: Define the anion gap:" How the anion gap can be calculated ? "

It is the difference between the sum of detectable cations (sodium and potassium) and anions (bicarbonate and chloride)

Q: A) What does high anion gap indicates? b)List the conditions where you can see high anion gap ?

A) Acidosis.

B) Renal disease, Diabetic ketoacidosis, Lactic acidosis, Poisoning.

Q: What are the clinical effect of acidosis:

1. Increased H+ conc. Stimulates respiratory response.
2. Hyperventilation: deep, rapid, and gasping respiratory pattern.
3. Arrhythmia, cardiac arrest.
4. Loss of consciousness , coma and death.

Q: Name the enzyme that convert pyruvate to lactate?

Lactate dehydrogenase enzyme

Q: List the causes of lactic acidosis?

1. Excessive tissue lactate production
2. Impaired hepatic metabolism of lactate

Q: What's the difference between the Type A and Type B of lactic acidosis ?

Type A : Occurs due to hypoxia in tissues,

Type B : Occurs due to disorders in carbohydrate metabolism.

Q: List 5 causes of type A lactic acidosis?

1. Myocardial infarction
2. Pulmonary embolism
3. Uncontrolled hemorrhage
4. Tissue hypoperfusion (shock, cardiac arrest, acute heart failure)
5. Anaerobic muscular exercise

Q: List 4 causes of type B lactic acidosis?

1. congenital deficiency of pyruvate dehydrogenase enzyme
2. Chronic hepatic disease accompanied by shock or bleeding
3. Liver failure
4. Drug intoxication

Q: How can we manage (treat) lactic acidosis?

1. Correcting the underlying conditions
2. Restoring adequate tissue oxygen
3. Avoiding sodium bicarbonate

Cholesterol metabolism

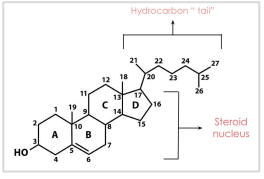
Q: Enumerate the functions of cholesterol:

- Maintains membrane fluidity.
- Insulating effect on nerve fibers.
- Parent molecule for bile acids and bile salts, steroid hormones, vitamin D_3.

Q: Cholesterol is the parent molecule of ?

Bile acids and bile salts, steroid hormones, vitamin D_3.

Just to help you memorize :)



Q: Describe the structure of free cholesterol ?

Steroid nucleus that has **4** hydrocarbon fused rings with a hydroxyl group at C3, double bond between C5&C6, hydrocarbon tail at C17 and a total of **27** carbons.

Q: Why is cholesteryl ester more hydrophobic than free cholesterol ?

Because there is a fatty acid attached to the site of hydroxyl group (C3)

Q: Enumerate the major sites of cholesterol synthesis:

1. Liver.
2. Adrenal cortex.
3. Testes and ovaries.
4. Intestine.

Q: What's the Rate limiting enzyme of cholesterol synthesis?

HMG- CoA **reductase**.

Q: Enumerate the mechanisms of HMG CoA reductase regulation ?

- Sterol-dependent regulation of gene expression.
- Sterol-accelerated enzyme degradation.
- Sterol-independent phosphorylation and dephosphorylation.
- Hormonal regulation.

Q: What's are the hormones that

A) Increase the upregulation of HMG CoA reductase expression? Insulin and thyroxine.

B) Decrease the upregulation of HMG CoA reductase expression? Glucagon and cortisol.

Q: What are the methods of treatment of hypercholesterolemia ?

1. Statin drugs (inhibit enzyme activity by competitive inhibition).
2. β-Sitosterols/phytosterols(block the absorption of dietary cholesterol).

Q: What are the major sources of liver cholesterol ?

1. Dietary cholesterol comes to liver in form of Chylomicron remnants.
2. De novo synthesis in the liver.
3. Cholesterol synthesized in extrahepatic tissues comes to liver in form of HDL.

Q: What are major routes by which cholesterol leaves the liver ?

1. Conversion to bile acids/salts.
2. Secretion of VLDL.
3. Free cholesterol secreted in the bile

Q: Where are the enzymes of cholesterol biosynthesis located ?

They are partly located in ER and partly in cytoplasm.

Q: Describe the role of AMPK in cholesterol synthesis:

When AMP is high , ATP will be low so AMPK will phosphorylate HMG-CoA reductase to decrease cholesterol synthesis.

Q: How is cholesterol excreted from the body ?

By conversion into bile acids and bile salts excreted in the feces :

- Direct secretion of cholesterol in bile.
- Transported to intestine for elimination and then will be converted there by bacteria into coprostanol and cholestanol before excretion.

Lipoprotein metabolism

Q: TAGs are mainly transported by ?
Chylomicrons and VLDL

Q: Cholesterol mainly transported by?
LDL and HDL

Q: The following apolipoproteins are present in:
a) Apo A-1? HDL
b) Apo B-48 ? Chylomicrons
c) Apo B-100 ? VLDL & LDL

Q: What does lipoprotein lipase require for activation?
- It requires Apo **C-II** for activation.

Q: What are the functions of Apolipoproteins ?
1. Provide structure to lipoproteins particles.
2. Provide recognition sites for cell- surface receptors.
3. Activators/Coenzymes for the enzymes involved in lipoprotein metabolism

Q: What's the difference between chylomicron and VLDL?
- Chylomicrons: Transport dietary TAGs to peripheral tissue, Assembled in the intestinal mucosal cells.
- VLDL: Composed of endogenous TAGs, Produced and secreted by the liver.

Q: Imbalance in hepatic TAG synthesis and secretion of VLDL can lead to?
Obesity and Type 2 diabetes mellitus

Q: VLDL transfers TAGs to HDL in exchange for cholesteryl esters This exchange is catalyzed by?
Cholesteryl ester transfer protein (CETP)

Q: What is the function of LDL and HDL ?
- LDL: transports cholesterol from the liver to the peripheral tissues.
- HDL: transports cholesterol from the peripheral tissues to the liver.

Q: What is the cause of **steatohepatitis (Fatty liver disease)** and its complication ?
- **Cause** : imbalance between TAGs synthesis in the liver and secretion of TAGs from the liver.
- **Complication** : will lead to accumulation of TAGs in the liver (fatty liver).

Q: What's the cause of **abetalipoproteinemia (Hypolipoproteinemia)** and its complication ?
- **Cause** : inability to load Apo **B** with lipids.
- **Complication** : Decrease the production of VLDLs and chylomicrons (Remember? they're made of Apo B-100 and Apo B-48 respectively), so TAGs will accumulate in the liver and intestine.

Q: What is the cause of **type 1 hyperlipoproteinemia** and its complication ?
- **Cause** : familial deficiency of LPL or is coenzyme apo **C-II** .
- **Complication** : will lead to excessive accumulation of chylomicrons in plasma (hyperchylomicronemia) and high fasting plasma TAGs are observed in these patients.

Q: What is the cause of **type 3 hyperlipoproteinemia (familial dysbetalipoproteinemia)** and its complication ?
- **Cause** : Individuals homozygous for apo **E-2** are deficient in clearing Chylomicron remnants and IDL from the circulation.
- **Complication** : Leads to hypercholesterolemia and premature atherosclerosis.

Q: Enumerate the types of lipoproteins:
1. Chylomicrons.
2. Very low density lipoprotein (VLDL).
3. Low density lipoprotein (LDL).
4. High density lipoprotein (HDL).

Lipoprotein metabolism , Contd..

Q: List the types of apolipoproteins:

1. Apo A-1
2. Apo B-48 , B-100.
3. Apo C-I , C-II , C-III.
4. Apo E.

Q: identify the marked area:
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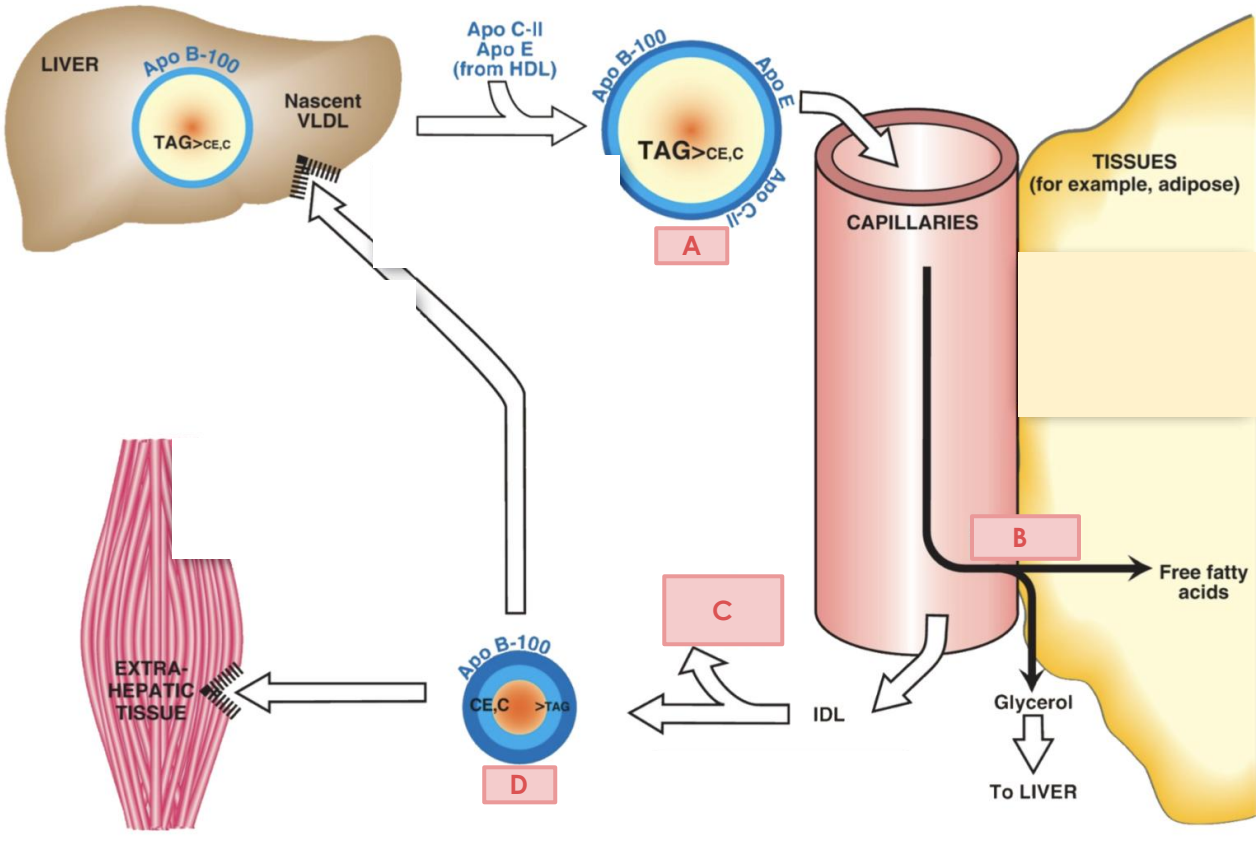


A- VLDL
B- Lipoprotein lipase
C- Apo C-II and apo E to HDL
D- LDL

Lipoprotein And Atherosclerosis

Q: How are low intracellular cholesterol levels regulated ?

1) Recycling of LDL receptors
2) Increase of receptor synthesis at gene level
3) Increase in cell surface receptors
4) Increased uptake of LDL by cells
5) Increased de novo synthesis of cholesterol

Q: How are high intracellular cholesterol levels regulated ?

1) Degradation of LDL receptors
2) Inhibition of receptor synthesis at gene level
3) Reduction in cell surface receptors
4) Decreased uptake of LDL by cells
5) Decreased de novo synthesis of cholesterol

Q: What are the characteristics of Nascent HDL ?

Disk-shaped, Mainly contains phospholipids, Contains apo **A-I**, **C-II** and E lipoproteins

Q: Apo A-I lipoprotein is found in?

HDL

Q: What's the difference between HDL and LDL ?

HDL	LDL
Good cholesterol	Bad cholesterol
Transports cholesterol from peripheral tissues to the liver for degradation	Transports cholesterol from the liver to peripheral tissues
High HDL levels decrease the risk for atherosclerosis & heart disease (inverse correlation with atherosclerosis)	High LDL levels increase the risk for atherosclerosis & heart disease (direct correlation with atherosclerosis)

Q: What's lipoprotein (a)?

Lipoprotein (a) is identical in structure to LDL particle and It contains Apo(a) in addition to apo B-100.

Q: Apo(a) protein is structurally similar to what protein and how does that influence its effect on the body?

Similar to plasminogen, so it competes with it and slows down the breakdown of blood clots therefore triggering heart attacks (it is a risk factor of coronary artery disease)

Q: What's the function of lipoprotein (a)?

- It competes with plasminogen to attack fibrin
- Slows the breakdown of blood clots.
- Triggering heart attack
- A risk factor for CAD

Q: Why LDL is considered a bad cholesterol ?

Because it increases the risk of atherosclerosis / heart disease.

Q: How the nascent HDL converted to HDL_3 ?

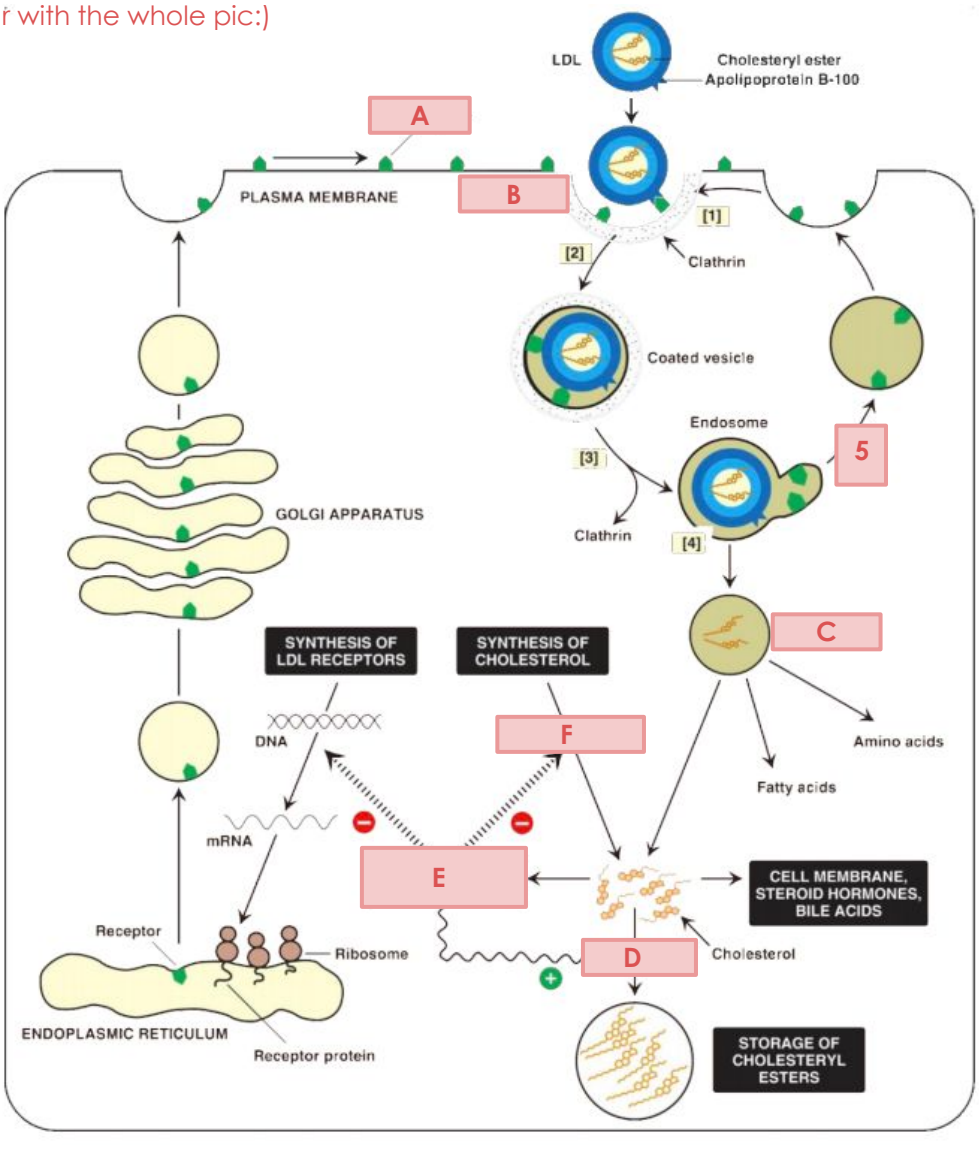
By adding a cholesteryl esters.

Lipoprotein And Atherosclerosis , Contd..

Q: What are the functions of HDL ?

1. Transports cholesterol to the liver from:
   - Peripheral tissues.
   - Cell membranes.
   - Other lipoproteins.
2. Suitable for cholesterol uptake due to:
   - High content of phospholipids.
   - Phospholipids will solubilize cholesterol and provide fatty acids for cholesterol esterification
3. Reservoir of apoproteins (Apo C-II and E).

Q: identify the marked area:
also be familiar with the whole pic:)



A- LDL receptor
B- Coated pit
C- Lysosome
D- ACAT (Acyl-CoA cholesterol acyltransferase)
E- Oversupply of cholesterol
F- HMG CoA Reductase (de-novo synthesis)

Q: What does step 5 represent?
Recycling of LDL receptor

Lipoprotein And Atherosclerosis , Contd..

Q: identify the marked area:
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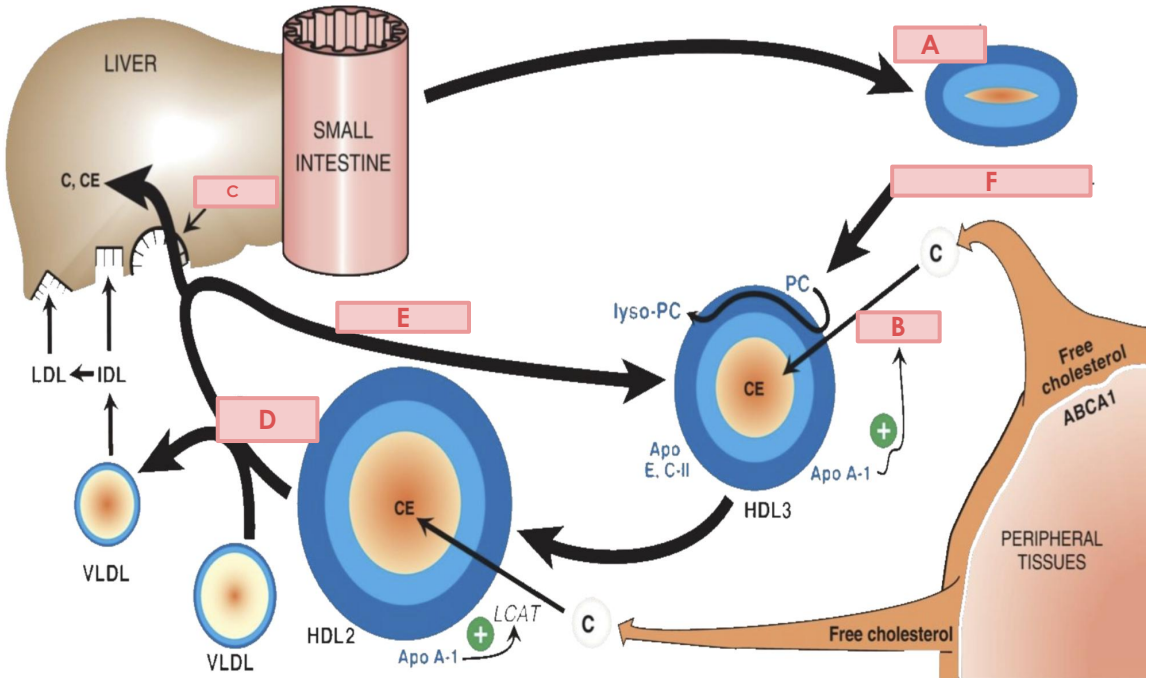


A- Apo A-I
B- LCAT (Lecithin-cholestrol acyltransferase)
C- SR-B1
D- CETP (cholesteryl ester transfer protein)
E- Hepatic lipase
F- Discoidal nascent HDL

Q: identify the marked area:
also be familiar with the whole pic:)

A: Name 4 oxidants in this figure that contributes in oxidizing LDL

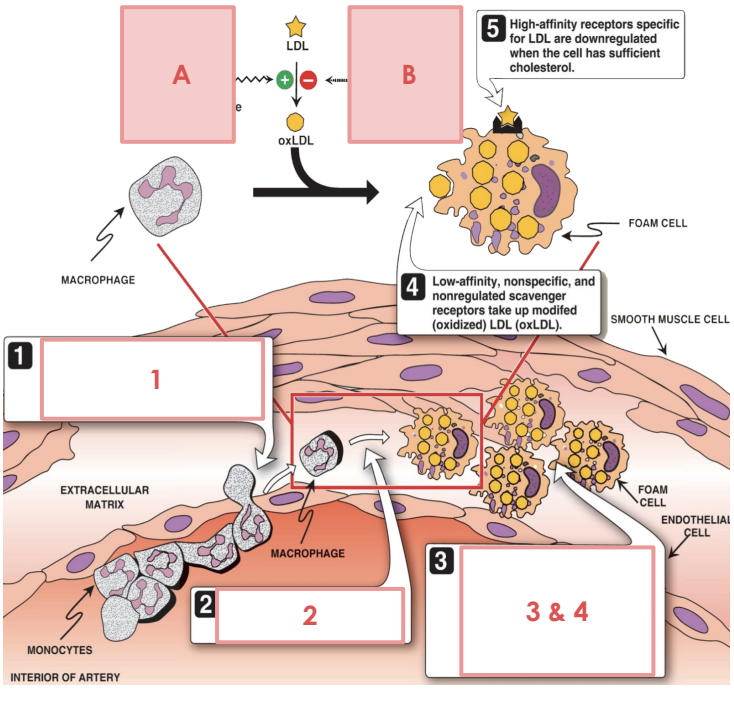
- Superoxide
- Nitric oxide
- Hydrogen peroxide
- Hydroxyl radical

B: Name 4 anti oxidants

- Vitamin A, C and E
- Beta carotene
- Glutathione system
- Superoxide dismutase
- Catalase

C: write the role of oxidized LDL in plaque formation

1. Endothelial injury & Monocyte adherence to endothelium and conversion to macrophages
2. Macrophages take up oxidized LDL by **SR-A receptor** becoming foam cells
3. SMCs migration to the concert from media to intima producing collagen and take up lipids and becoming foam cells
4. Foam cell accumulation → atherosclerotic plaque



Oxidative stress

Q: What are the oxidative stress ?

Oxidative stress is a condition in which cells are exposed to excessive levels of:

- Reactive Oxygen Species (ROS).
- Reactive Nitrogen Species (RNS).

Q: Mention 3 diseases caused by oxidative stress.

Atherosclerosis, Coronary artery disease, Obesity, Cancer, Inflammatory diseases (rheumatoid arthritis), G6PD deficiency hemolytic anemia
(oxidative stress is also involved in aging)

Q: Reactive Oxygen Species (ROS) are continuously formed by "their source"?

- Partial reduction of molecular oxygen in ETC.
- As byproducts of aerobic metabolism.
- Ingestion of drugs, toxins, chemicals.
- When cellular antioxidant level is low.
- Creating oxidative stress in cell.

Q:What are the target for ROS ?

- DNA, proteins, unsaturated lipids

Q: Q: identify the marked area:
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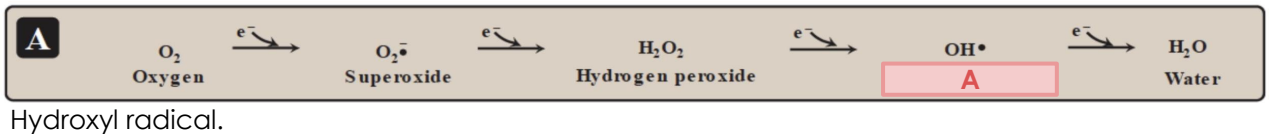

A) Hydroxyl radical.

Q: identify the marked area:
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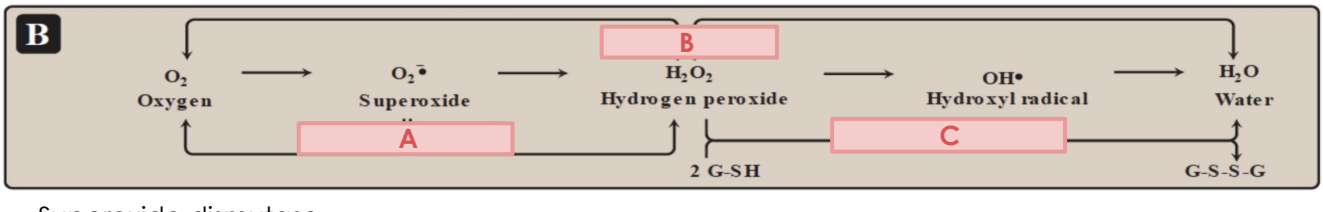

A) Superoxide dismutase.
B) Catalase.
C) Glutathione peroxidase.

Q: Enumerate 4 antioxidants?

- Enzymes: Superoxide dismutase, Catalase, Glutathione system.
- Vitamins: Vitamins A, C, E and β-Carotene

Q: Enumerate 4 effects of ROS :

- DNA damage.
- Protein denaturation.
- Cytoskeletal damage.
- Increased endothelial cell permeability.
- Altered vascular tone.

Q: Reduced glutathione consist of?

- glycine, cysteine , glutamate

Q: Glucose-6-phosphate dehydrogenase(G6PD) deficiency can lead to?

- NADPH deficiency (resulting in **hemolysis**).
- Cells are unable to reduce free radicals.
- Oxidation of cellular proteins is increased causing impaired cell function.

Q: Nitric Oxide (NO) is produced by?

- Nitric oxide synthase

Oxidative stress, Contd..

Q: What are the members of glutathione system ?

1. Glutathione reductase.
2. Glutathione peroxidase.
3. NADPH.

Q: What is the mechanism of glutathione system ?

It uses **NADPH** to reduce **oxidized glutathione(G-S-S-G)** to the **reduced state(2 G-SH)** by the enzyme **glutathione reductase**, which is then used to reduce **hydrogen peroxide** into **water** by the enzyme **glutathione peroxidase**.

Q: What's the role of G6PD ?

G6PD is used to restore the NADPH from the oxidized $NADP^+$.

Q: identify the marked area:
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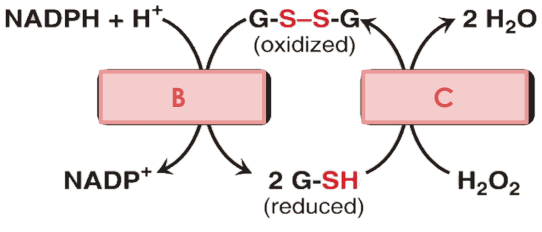
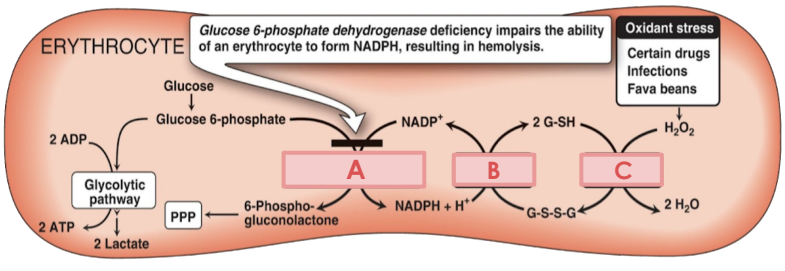




A) G6PD (Glucose 6-phosphate dehydrogenase).
B) Glutathione reductase.
C) Glutathione peroxidase.

Q: What are the different types of nitric oxide synthase ?

1. eNOS in the endothelium (vaso-relaxation).
2. nNOS in the neural tissue (neurotransmission).
3. iNOS in macrophages, neutrophils (infection).
4. bNOS (bacterial).

Q: When does iNOS increase and how can it damage body cells ?

· During infections, they will cause more production of free radicals which will lead to oxidative stress.

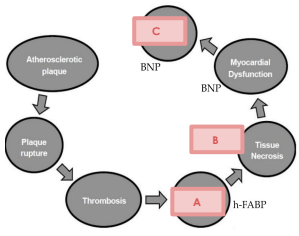
Biochemical Markers of Myocardial Infarction

Q: What's the pathogenesis of MI " What's happening in MI ? "

1. Occlusion of coronary arteries.
2. Restricted blood supply (oxygen) to heart tissue (ischemia).
3. Damage to heart tissue (infarction).
4. Release of enzymes and other proteins into the blood (markers).

Q: identify the marked area:
also be familiar with the whole pic:)

A) Tissue ischemia.
B) cTn and CK-MB.
C) Heart failure.



Q: Enumerate 5 features Of An Ideal Cardiac Marker ?

- High concentration in the myocardium.
- High sensitivity.
- High specificity
- Rapid release into plasma following myocardial injury.
- Good prognostic value.
- Easily measured.

Q: What are CURRENT markers of diagnostic value in **MI** ?

- Cardiac troponin T (cTnT).
- Cardiac troponin I (cTnI).
- Creatine kinase-MB (CK-MB).

Q: Mention 1 marker of diagnostic value in **HEART TISSUE ISCHEMIA** ?

- Heart fatty acid binding protein (h-FABP).

Q: Mention 1 marker of diagnostic value in **HEART FAILURE**?

- B-type natriuretic peptide (BNP).

Q: Mention 1 marker that is useful for diagnosis of **re-infarction** ?

- Creatine kinase-MB (CK-MB).

Q: list the advantages and disadvantages for using **CK-MB** in diagnosing **MI** ?

- Advantages:
  - Useful for early diagnosis of MI.
  - Useful for diagnosis of **re-infarction**.
- Disadvantages:
  - Not significant if measured after 2 days of MI (delayed admission).
  - Not highly specific (elevated in skeletal muscle damage).

Q: Regarding cardiac troponins and CK-MB state the following :

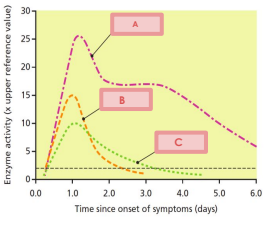
A) After MI, how long do they take for troponins and CK-MB to be detectable in the blood ?
Troponins take 4-6 h and CK-MB takes 3-10h (CK-MB can be measured first).

B) How long do they take to reach its peak value?
Troponins and CK-MB take 12-24 h.

C) Duration for which they remain abnormal?
Troponins 3-10 days and CK-MB 1.5-3 days (Troponins can be measured after a long period of time).

Q: Q: identify the marked area:

A) Troponin
B) CK-MB
C) Total CK



Q: Define the lag phase?

- It's the duration between damage and release of markers

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