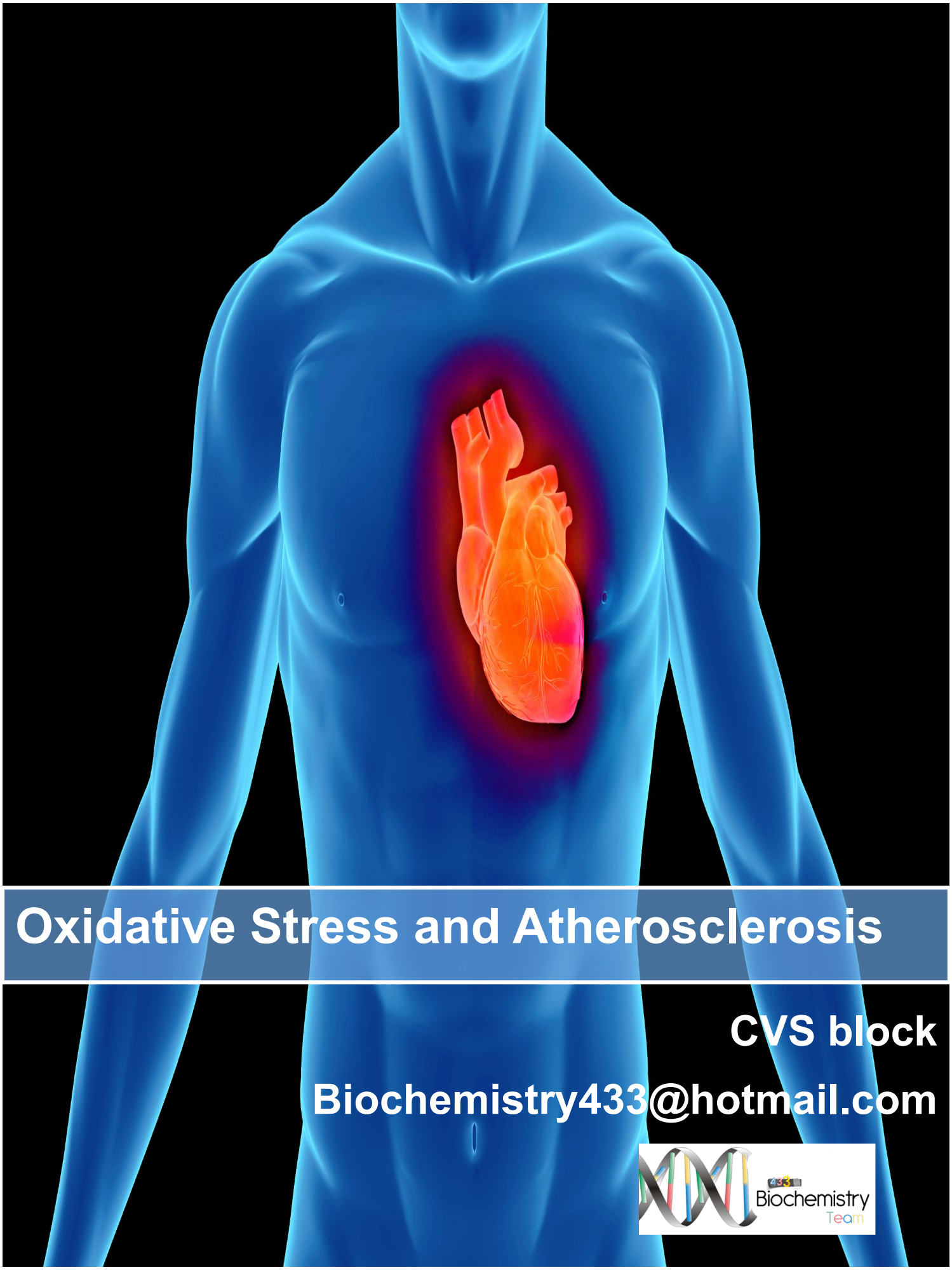

Oxidative Stress and Atherosclerosis

CVS block

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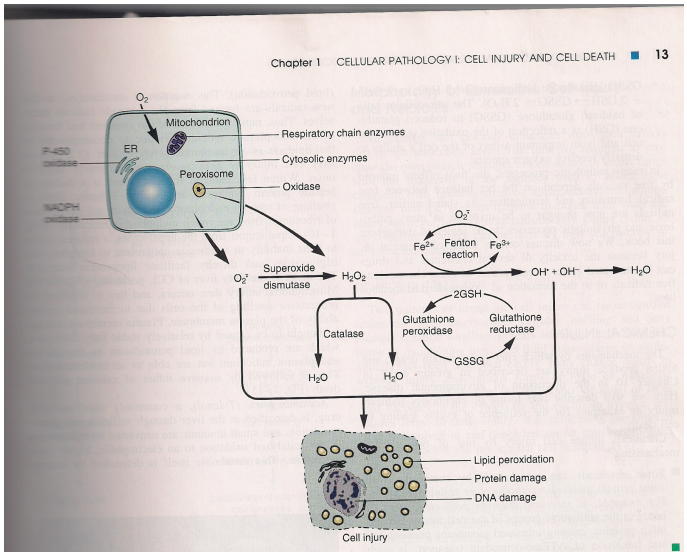
Oxidative stress

- A condition in which cells are subjected to excessive levels of Reactive Species (Oxygen or Nitrative species) & they are unable to counterbalance their deleterious effects with antioxidants.
- It has been implicated in the ageing process & in many diseases (e.g., atherosclerosis and coronary heart diseases).

Imbalance between oxidant production and antioxidant mechanisms



Oxidative damage to:

- DNA
- Proteins
- Lipids (unsaturated fatty acids)

(double bonds makes it weaker and more vulnerable to injuries)

Oxidative stress and diseases:

- Inflammatory conditions e.g., Rheumatoid arthritis
- Atherosclerosis and coronary artery diseases
- Obesity
- Cancers
- G6PD deficiency hemolytic anemia
- Diabetes Mellitus

Free radicals: presence of an impaired electron in the outer orbid of an atom

Reactive Oxygen Species (ROS)

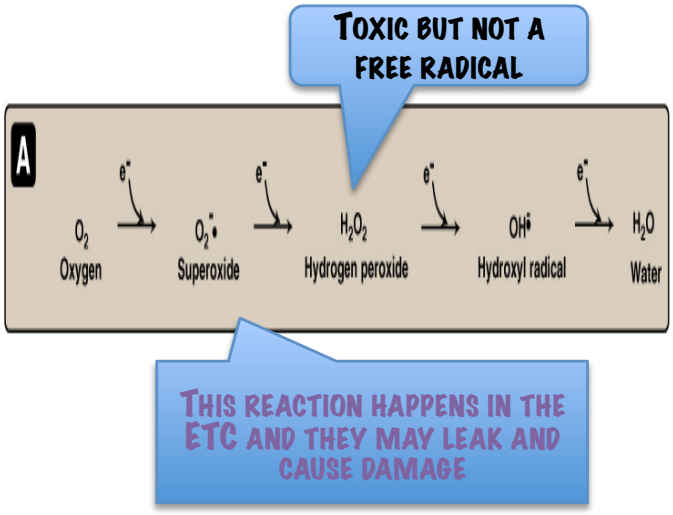
Types:

- Free radical:

Superoxide (O2.) (oxygen derived)
Hydroxyl radical (OH.) (oxygen derived)
Peroxyl radical (ROO.)

- Non free radical:

Hydrogen peroxide (H2O2)



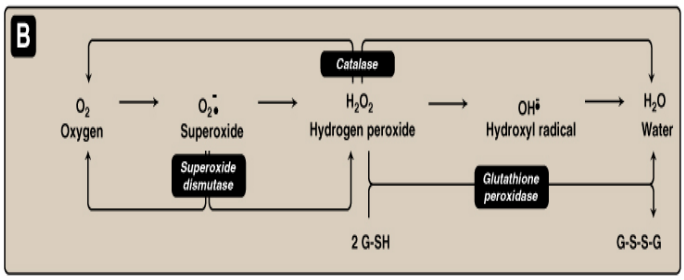
- Sources:
- During course of metabolism

E.G.,

O_2 by auto-oxidation of hemoglobin and xanthine oxidase
OH by Fenton reaction
$O_2^{\cdot-}$, H_2O_2, OH by partial reduction of molecular oxygen in electron transport chain in mitochondria

- Ingestion of toxins, chemicals or drugs

Antioxidant Mechanisms



Enzymes:

- Superoxide dismutase
- Catalase
- Glutathione system (glutathione, NADPH, reductase, peroxidase & selenium)

Vitamins:

- Vitamin C (ascorbic acid)
- Vitamin A and β-carotenes
- Vitamin E

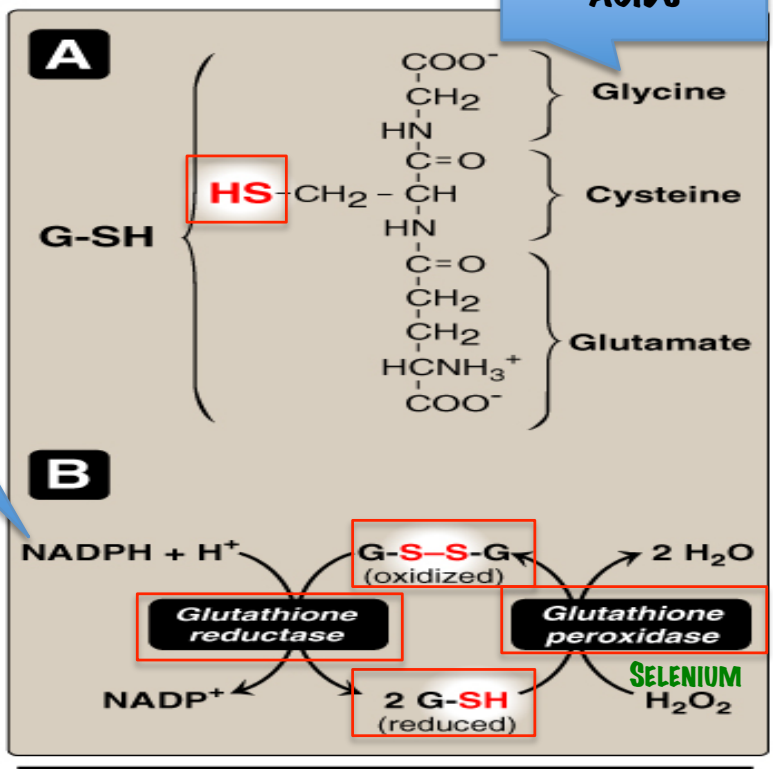
Trace elements:

- Selenium

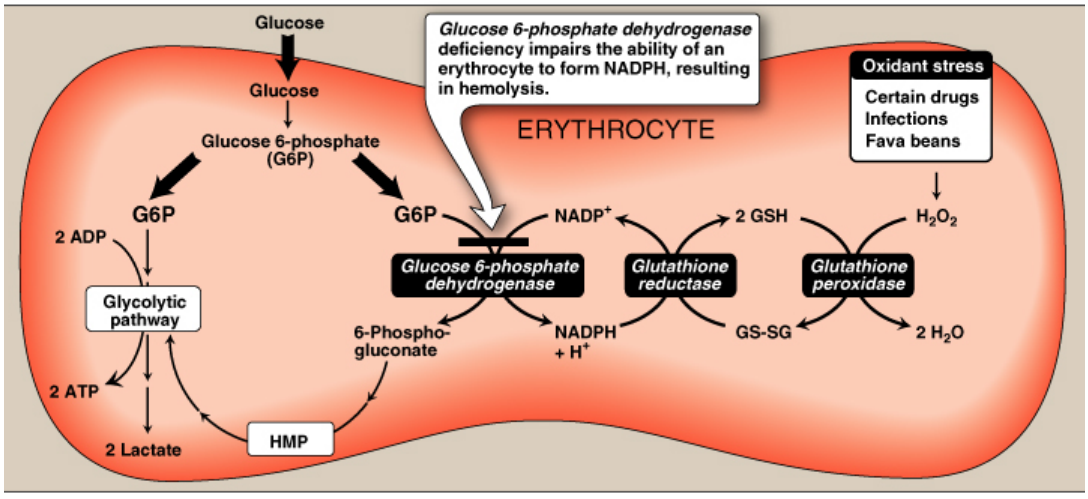
Glutathione System

3 AMINO ACIDS

GLUCOSE-6-PHOSPHATE DEHYDROGENASE (G-6-PD) IS THE MAIN SOURCE FOR NADPH GENERATION AND IS, THEREFORE, ESSENTIAL FOR PROPER FUNCTION OF GLUTATHIONE SYSTEM



Biochemical Basis of G6PD Deficiency Hemolytic Anemia



Molecular & Vascular Effects of ROS

Molecular effects:

- Lipid peroxidation (polyunsaturated fatty acids)
- Protein denaturation
- Inactivation of enzymes
- DNA damage
- Cell signaling effects
  (e.g., release of Ca2+ from intracellular stores)
- Cytoskeletal damage
- Chemotaxis

Vascular effects:

- Altered vascular tone
- Increased endothelial cell permeability

Nitric Oxide (NO)

NO:

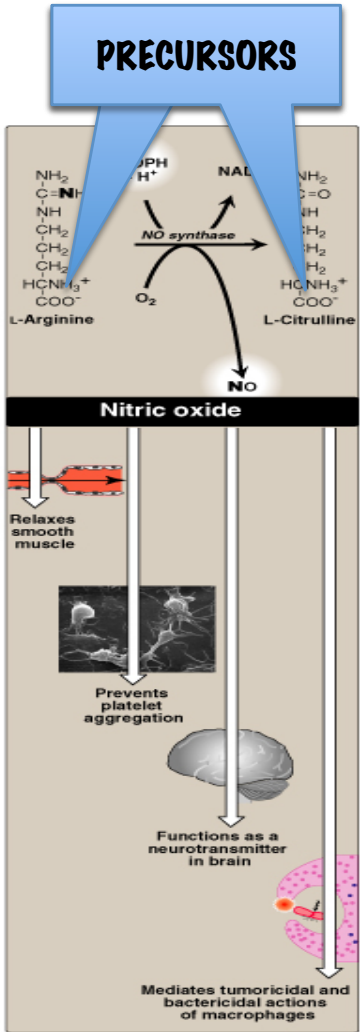
Free radical gas (not oxygen derived)
Very short half-life (seconds)
Metabolized into NITRATES & NITRITES (by measuring them we can find the values if NO)

Synthesis:

Enzyme: NO synthase (NOS)
Precursor: L-Arginine

Effects:

Relaxes vascular smooth muscle
Prevents platelet aggregation
Bactricidal & Tumoricidal effects
Neurotransmitter in brain



Oxidative Stress: Role of Nitric Oxide (NO)

- This may be both beneficial and detrimental, depending upon when and where NO is released

- NO produced by endothelial NOS (eNOS) → improving vascular dilation and perfusion (i.e., BENEFICIAL).

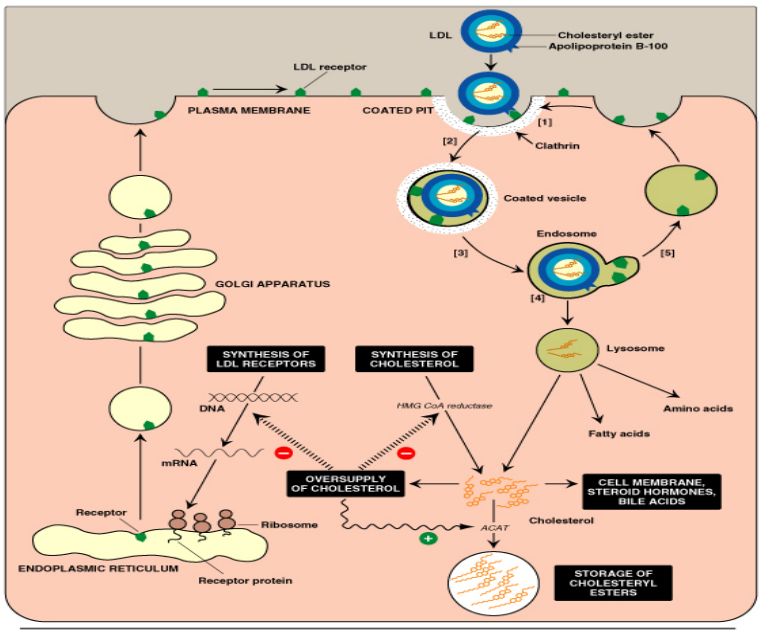
- Vasodilators such as nitroglycerin is metabolized into NO and causes vasodilatation

- In contrast, NO production by neuronal NOS (nNOS) or by the inducible form of NOS (iNOS) has been reported to have detrimental effects.

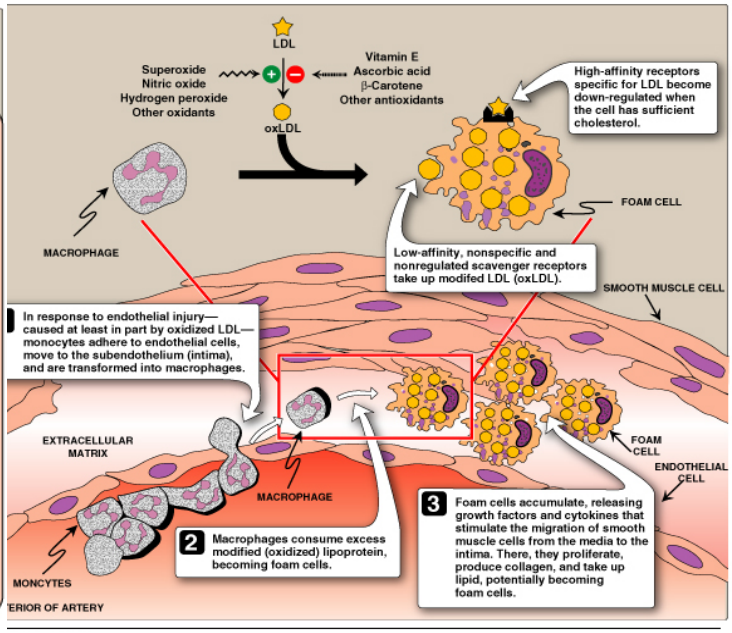
- Increased iNOS activity is generally associated with inflammatory processes

Pathogenesis of Atherosclerosis

- Modified (oxidized) LDL … Oxidative stress
  (imbalance between oxidants and antioxidants)
- Endothelial injury of arterial wall
- Adherence of monocytes to endothelial cells and their movement into intima where it becomes macrophages
- Uptake of oxLDL by macrophage scavenger receptor:
  Scavenger receptor class A (SR-A)
  - ➲ Low-affinity, non-specific receptor
  - ➲ Un-regulated receptor
- Foam cell transformation: Accumulation of excess lipids inside the cells (unregulated receptor)
- Atherosclerotic plaque formation



LDL: Receptor-Mediated Endocytosis



Atherosclerotic plaque formation

QUIZ YOURSELF!!

1- WHICH OF THE FOLLOWING IS A NON-FREE RADICALS?
A- HYDROGEN PEROXIDE
B- HYROXYL RADICALS
C- SUPEROXIDE

2- WHICH OF THE FOLLOWING IS A POSSIBLE RESULT FROM HYMOLYTIC ANEMIA?
A- NADPH DEFIENCY
B- FAD DEFIENCY
C- REDUCTASE DEFIENCY

3- WHICH OF THE FOLLOWING IS CONSIDERED AS A SOURCE OF REACTIVE OXYGEN SPECIES (ROS)?
A- PEROXYL RADICAL
B- INGESTION OF DRUGS
C- CARGOHYDRATE INTAKE

4- GLUATATHIONE SYSTEM IS CONSIDERED AS A?
A- OXIDANT PRODUCTION
B- VASCULAR EFFECTOR
C- ANTI-OXIDANT AGENT

5- WHICH OF THE FOLLOWING IS A RESULT FROM AUTO-OXDIATIVE HEMOGLOBIN?
A- SUPEROXIDE
B- HYDROGEN PEROXIDE
C- PEROXYL REDICAL

ANS: 1- A 2- A 3- B 4- C 5- A

GOOD LUCK!!

FROM OUR TEAM MEMBERS:

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AHMAD ALHUSSAIN
ZIYAD ALAJLAN