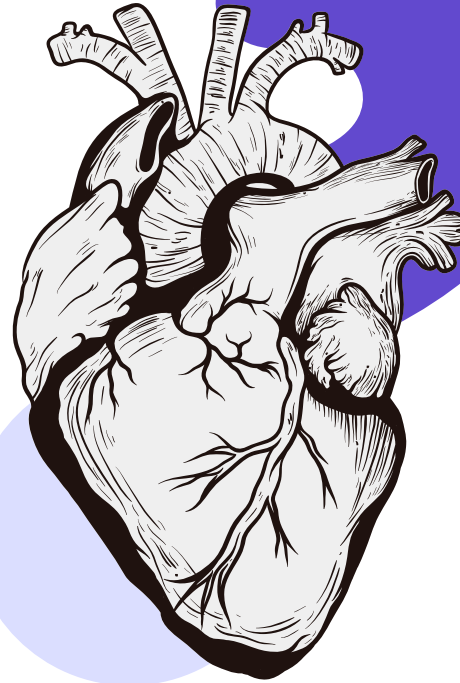


Oxidative stress



Editing File

COLOR INDEX:

MAIN TEXT (BLACK)

FEMALE SLIDES (PINK)

MALE SLIDES (BLUE)

IMPORTANT (RED)

DR'S NOTE (GREEN)

EXTRA INFO (GREY)

Objective

01

Define oxidative stress.

03

Understand the harmful effects of oxidative stress to the cell and its diseases.

05

List the types, sources and effects of Reactive Oxygen Species (ROS).

02

List various antioxidants in the body.

04

Understand the role of glutathione system in detoxifying oxidants in the body.

06

Discuss how G6PD deficiency leads to oxidative stress.

04

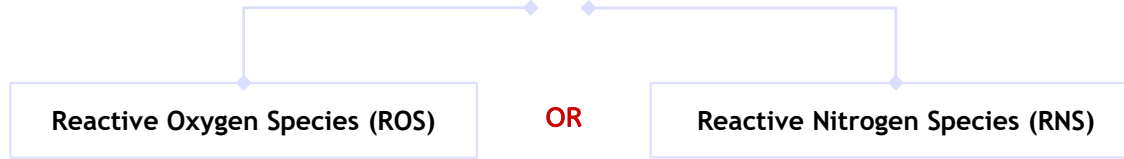
Understand the role of Reactive Nitrogen Species (RNS) in contributing to oxidative stress.

06

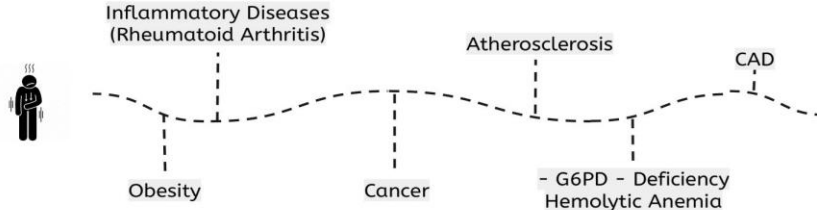
Correlate the role of oxidative stress to pathogenesis of atherosclerosis.

Oxidative Stress

- A condition in which cells are exposed to excessive levels of :



- Cells are **unable** to neutralize their deleterious effects with antioxidants.
- Oxidative stress is implicated in atherosclerosis, CAD (Coronary artery disease), ageing.
- Cellular imbalance of oxidants and antioxidants **damages**: DNA, proteins, lipids.
- Diseases due to oxidative stress :



Note 439: they're produced normally in the cells, and we have a system to take care of these species which is (Antioxidant Machinery) but if the production of these reactive species is too much, our antioxidant machinery will not work sufficiently, also if there's inflammation in the body it will lead to oxidative stress.

Reactive Oxygen Species (ROS)

- Incomplete reduction of oxygen to water produces ROS.

They are present at low and stationary level in normal cells

- ROS are continuously formed : 

- As byproducts of **aerobic** metabolism.
- Thru reactions with drugs and toxins.
- When cellular antioxidant level is **low**.
- Creating oxidative stress in cell.

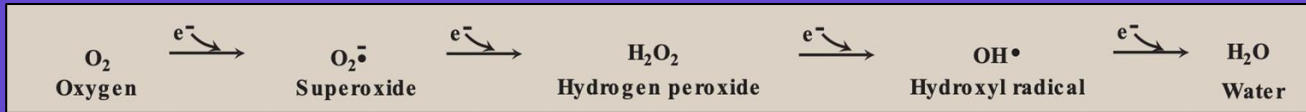
why unsaturated?
because they contain double bond in which the electron share is weaker

- ROS can damage DNA, proteins, unsaturated lipids → Cell Death
- Cells have **protective antioxidant mechanisms** that neutralize ROS.

★ Reactive Oxygen Species (ROS)

A

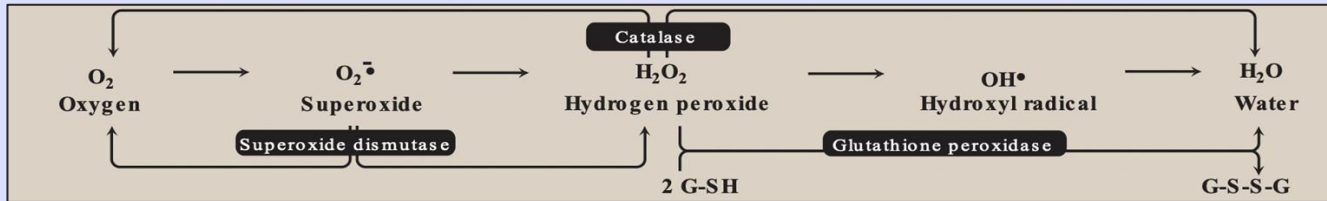
Formation of reactive intermediate from molecular oxygen :



We need 4 e⁻ to produce water
And we need 2 e⁻ to produce hydrogen peroxide

B

Actions of antioxidant enzymes :



Note 443:

G-SH : Reduced glutathione.

G-S-S-G : Oxidized glutathione.

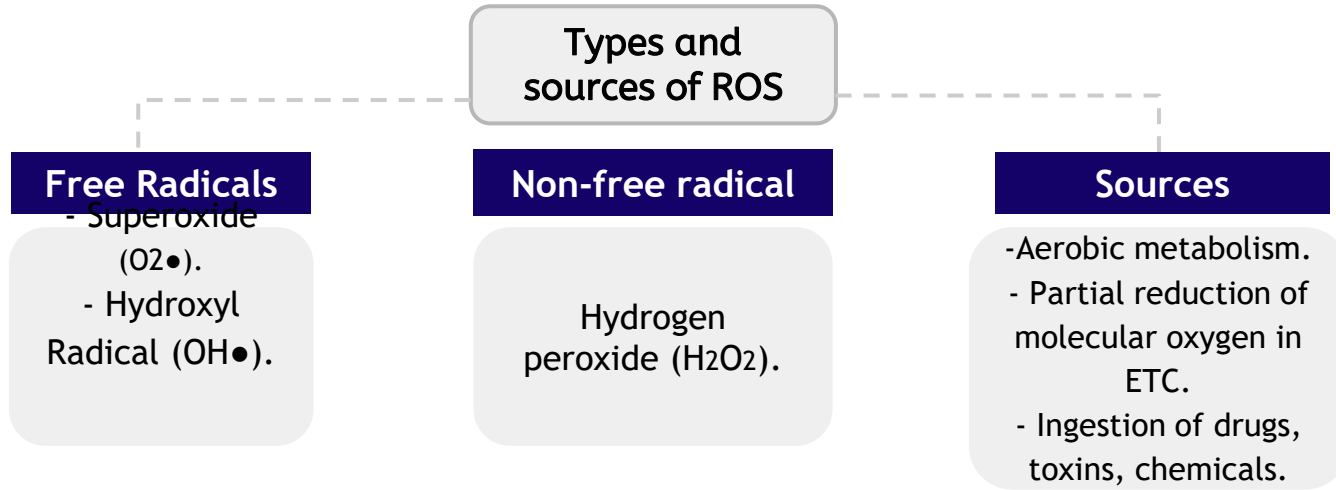
Hydrogen peroxide : Can be converted to H₂O either directly by catalase or indirectly by glutathione peroxidase.

Superoxide : Is converted to O₂ by superoxide dismutase

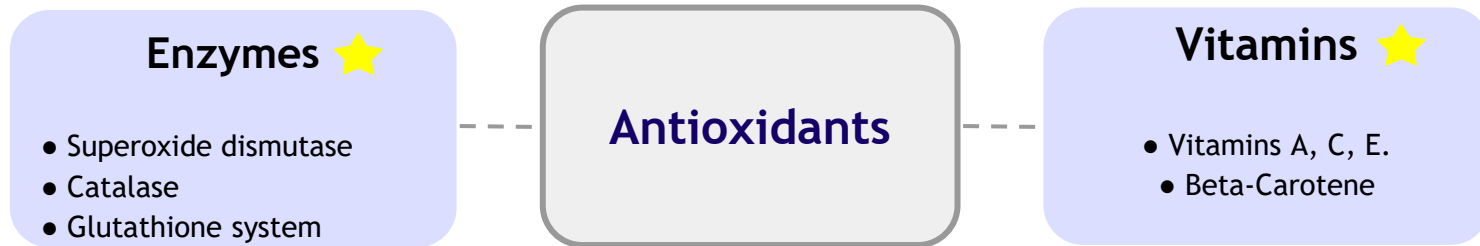
The problem begins when the reduction of oxygen to water stops at Superoxide, Hydrogen peroxide or Hydroxyl radical.

one or two of these ROS will accumulate in our body and cause diseases.

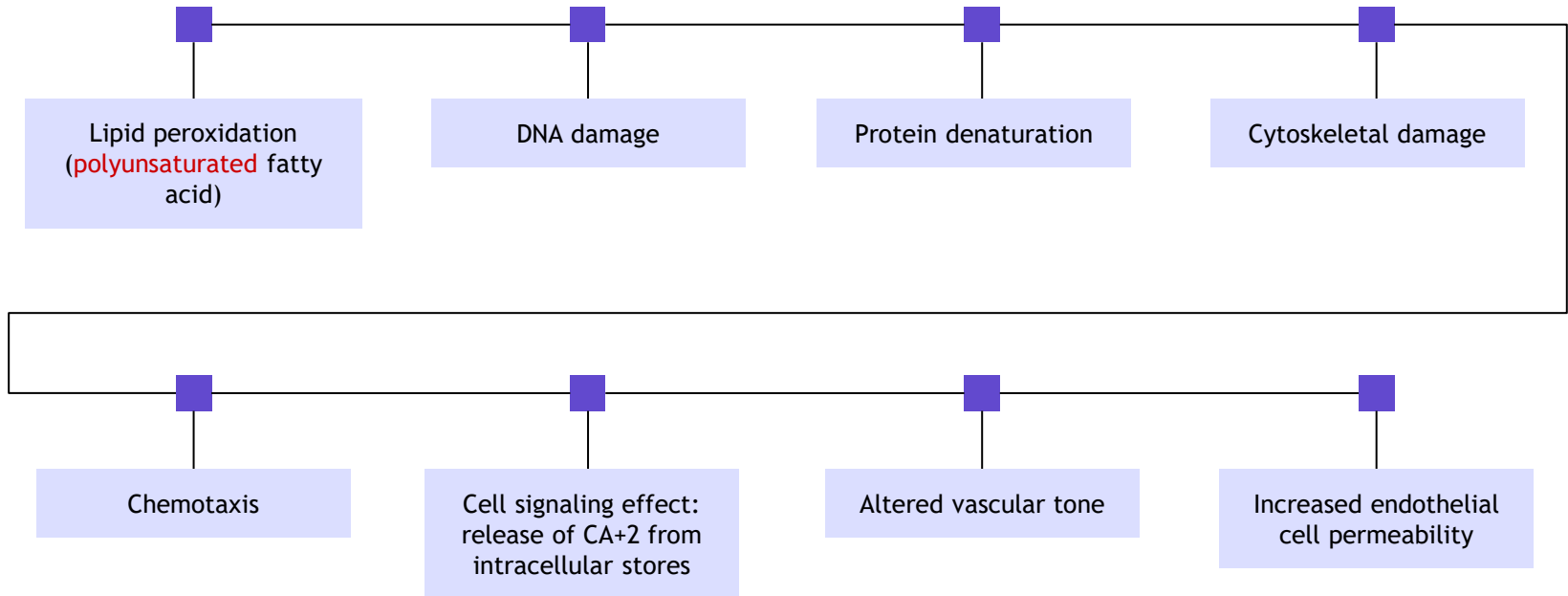
Types and Sources of ROS



Antioxidants



Effects of ROS



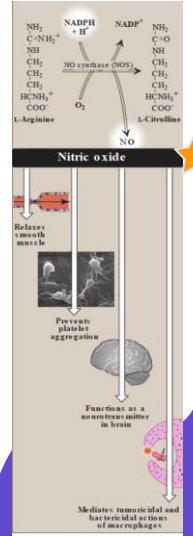
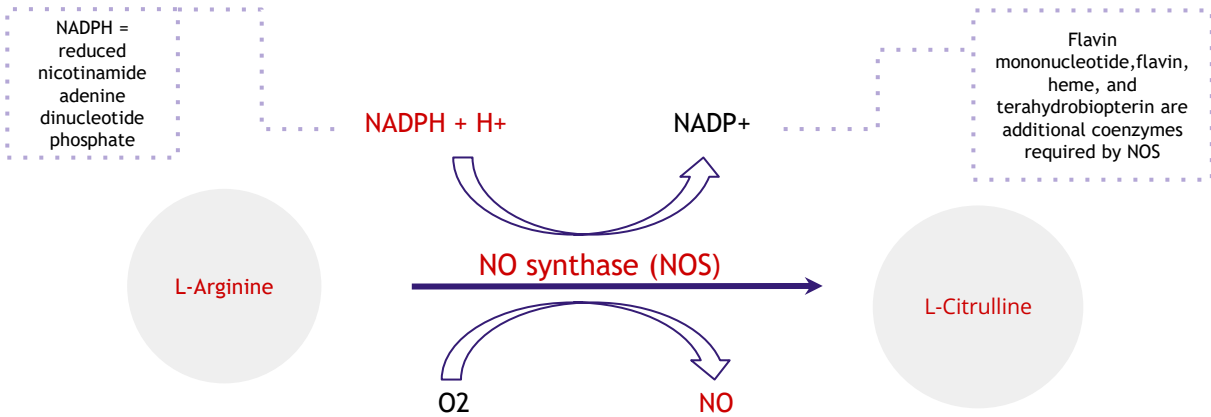
Nitric oxide (NO)

- 1 Endothelial-derived relaxing factor
- 2 Causes vasodilation by relaxing vascular smooth muscle
- 3 NO is a gas with short half-life (3-10 sec)

Reactive nitrogen species

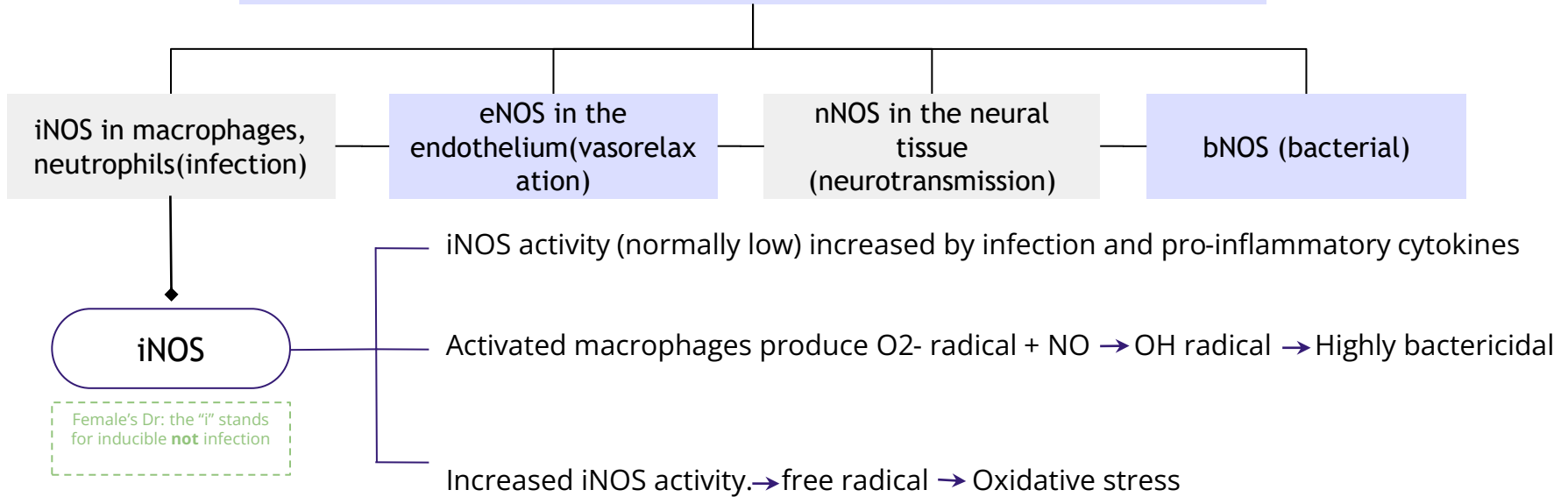
NO + oxygen/superoxide → Nitrites, Nitrates, **Peroxynitrite** (O=NOO-)
Peroxynitrite is a reactive nitrogen species (RNS)

Nitric oxide synthesis

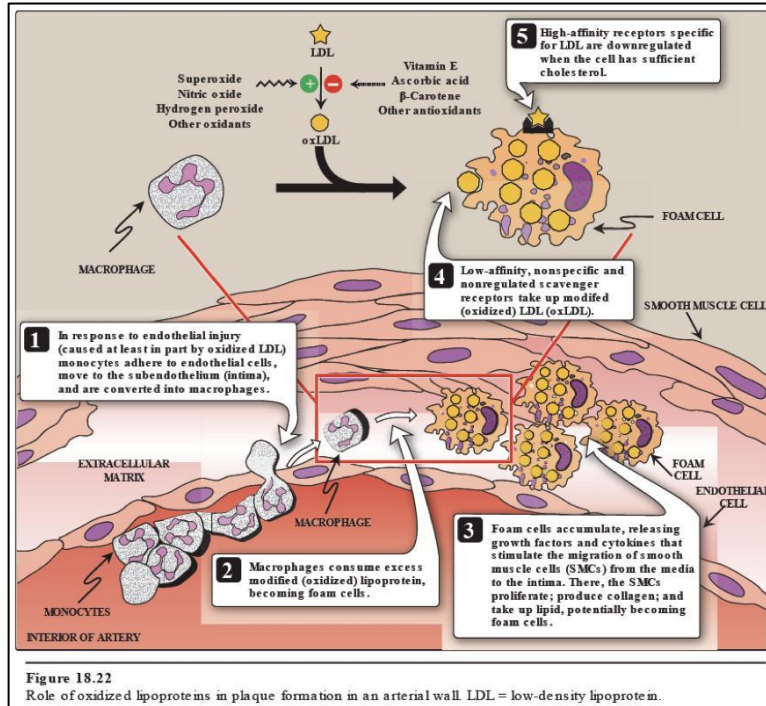


Nitric oxide cont.

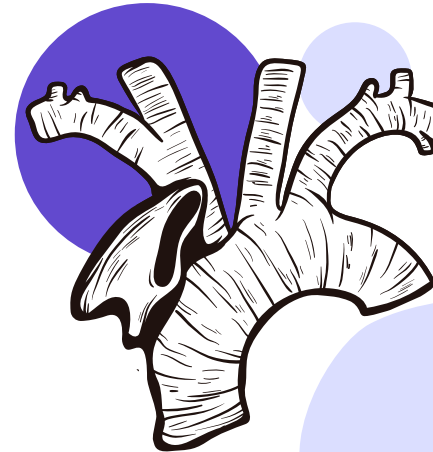
NO is produced by nitric oxide synthase
(which have different isoenzymes)



Oxidative stress and atherosclerosis



the basic cause of atherosclerosis is plaque formation, plaque is made of the accumulation of foam cells, and they are produced by eating up all the lipids but what are the lipids that they take in? basically as it was mentioned earlier ROS targets DNA, proteins and lipids, so when they target LDL molecule they lead to the production of oxidized LDL (modified form of LDL), so when there are excessive amounts of ROS, LDL is going to be oxidized → gets taken by macrophages → formation of foam cell



Take Home Messages

- Oxidative stress is due to excessive production of ROS and NOS in the cells.
- Cells neutralize these oxidants by a number of antioxidant processes.
- Imbalance between oxidants and antioxidants in the cells can result in the development of many diseases including atherosclerosis.

Q1: Which of the following is produced by the addition of three electrons to oxygen, and it is considered the most harmful free radical?

A-Water

B-Superoxide

C-Hydrogen peroxide

D- Hydroxyl radical

Q2: superoxide dismutase is an antioxidant enzyme that turns the superoxide into?

A-water

B-hydroxyl radical

C-nitric oxide

D-hydrogen peroxide

Q3: what is the most virulent to be damaged by free radicals?

A-DNA

B-rRNA

C-mRNA

D-tRNA

Q1: which one of the following is not a part of the glutathione system?

A-selenium

B-NADPH

C-catalase

D-glutathione reductase

Q2: which one of the following is caused by G6PD deficiency ?

A-excessive amount of NADPH

B-oxygen equilibrium

C-reduce free radicals

D- increased endothelial cell permeability

Q3: which enzyme is essential for the proper function of glutathione system?

A-lipoprotein lipase

B-HMG COA reductase

C-NO synthase

D-G6PD

SAQ

Q1: How ROS are continuously formed?

A1: Slide 4

Q2: What are the actions of (NO)

A2: Slide 9

Q3: Enumerate FOUR antioxidants in the cell

A3:
Vitamin A,C,E
B-carotene
Superoxide dismutase
Catalase

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