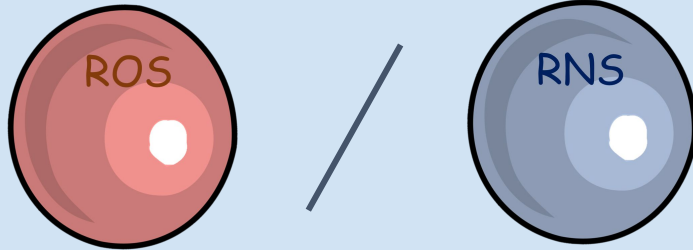






Oxidative Stress



-  Main text
-  Important
-  Notes
-  Extra

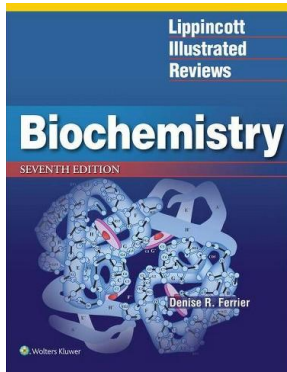
[Editing File](#)

We recommend that to watch this video below to get general idea about this lecture & we suggest this book for you if you want more details



Reactive Oxygen Species and oxidative stress

By Animated biology With arpan



Biochemistry Lippincott Illustrated Reviews 7th Edition

BY Denise R. Ferrier

Chapter 13
Pages 638-665



Objectives

- ◆ Define oxidative stress.
- ◆ Understand the harmful effects of oxidative stress to the cell and its diseases.
- ◆ List the types, sources and effects of Reactive Oxygen Species (ROS).
- ◆ List various antioxidants in the body.
- ◆ Understand the role of glutathione system in detoxifying oxidants in the body.
- ◆ Discuss how G6PD deficiency leads to oxidative stress.
- ◆ Understand the role of Reactive Nitrogen Species (RNS) in contributing to oxidative stress .
- ◆ Correlate the role of oxidative stress to pathogenesis of atherosclerosis.



Oxidative stress

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

→ Reactive Oxygen Species (ROS) is Formed by the help of oxygen .

Or.

→ Reactive Nitrogen Species (RNS) is formed by the help of Nitrogen .

- Cells are unable to neutralize their deleterious effects with antioxidants.
- Oxidative stress is implicated in atherosclerosis, CAD, ageing.
- Cellular imbalance of oxidants and antioxidants damages: DNA, proteins, lipids.



ROS and RNS are physiologically present but they get removed by antioxidant. If an imbalance occurs it becomes pathological.

Disease due to oxidative stress:

Inflammatory diseases
(rheumatoid arthritis)

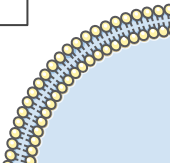
Atherosclerosis

CAD

Obesity

Cancer

G6PD deficiency hemolytic
anemia

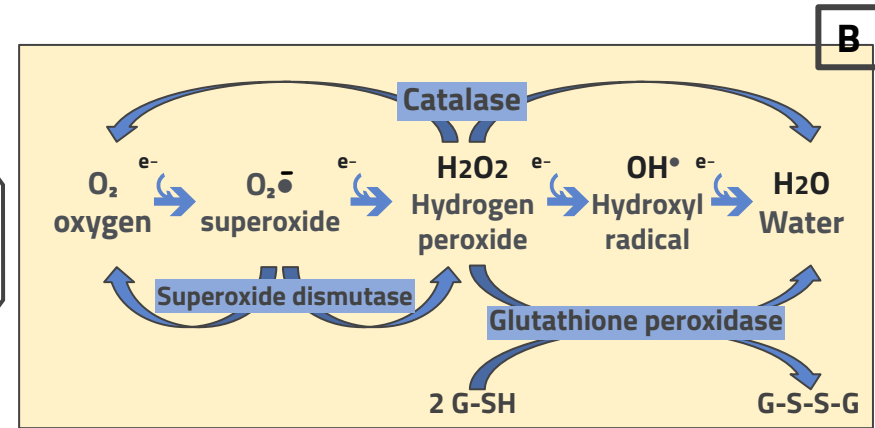
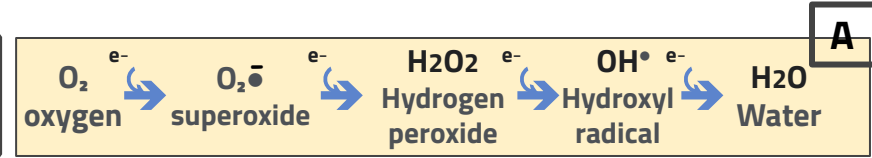


Reactive Oxygen Species (ROS)



Oxidation is the **loss** of electrons during a reaction.
Reduction is the **gain** of electrons during a reaction.

- **Incomplete** reduction of oxygen to water produces ROS.
- **ROS** can damage DNA, proteins, unsaturated lipids → cell death.
- Cells have protective antioxidant mechanisms that neutralize **ROS**.
- ROS are continuously formed :
 - As byproducts of aerobic metabolism .
 - Thru reactions with drugs and toxins .
 - When cellular antioxidant level is low **Increase oxidation or Decrease antioxidant**.
 - Creating oxidative stress in cell.

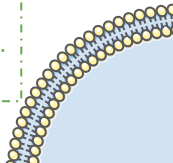


G-SH: Reduced glutathione.
G-S-S-G: Oxidized glutathione .
Hydrogen peroxide: Can be converted to H₂O either directly by catalase or indirectly by glutathione peroxidase .
Superoxide: Is converted to O₂ by superoxide dismutase.

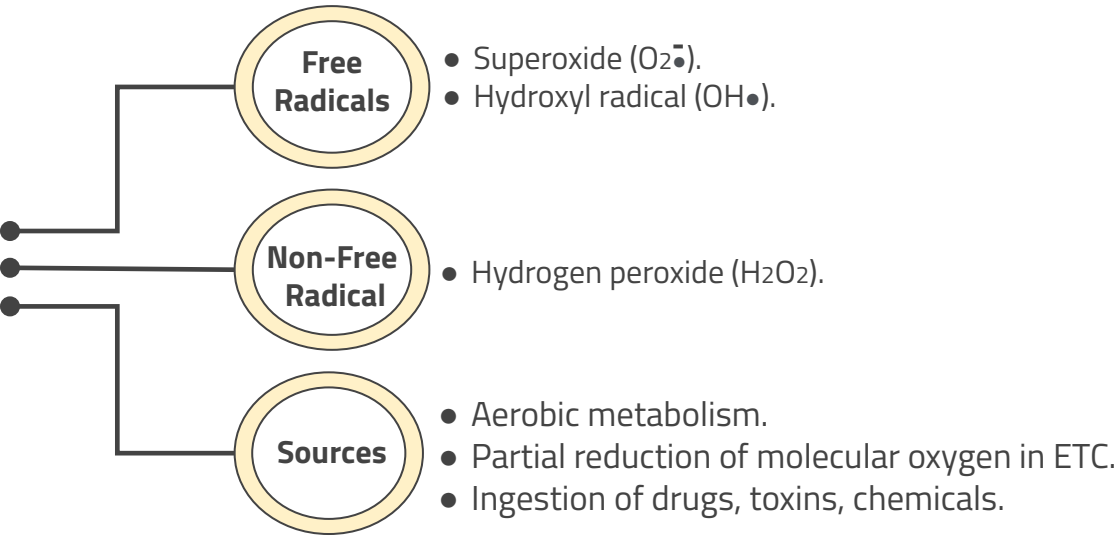


المشكلة بالعملية ذي نوعين :
 ١- مشكلة بالـ Enzymes
 ٢- زيادة في الـ Radicals
 لدرجة ان الـ Enzymes ما تقدر تتخلص منها
 النتيجة؟

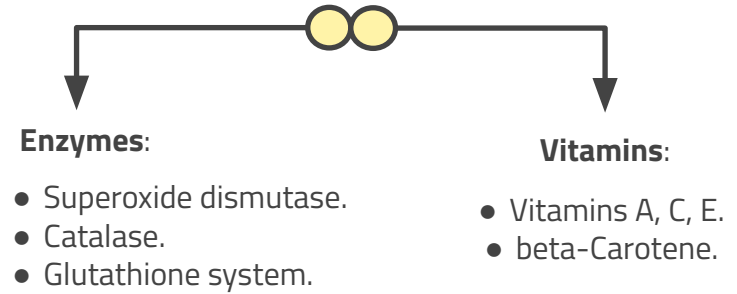
Increase in radicals that lead to LDL oxidation and therefore Atherosclerosis



Types and sources of ROS

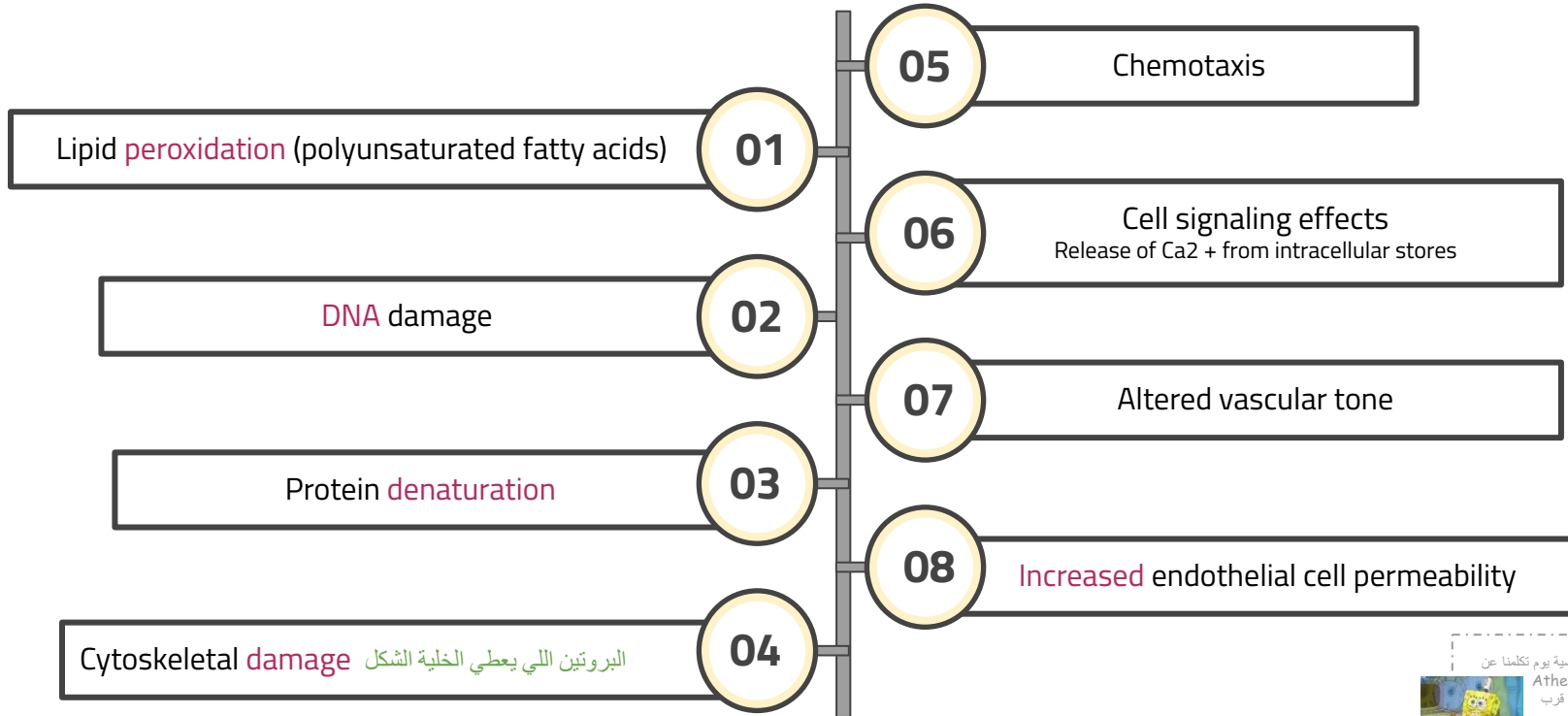


Antioxidants





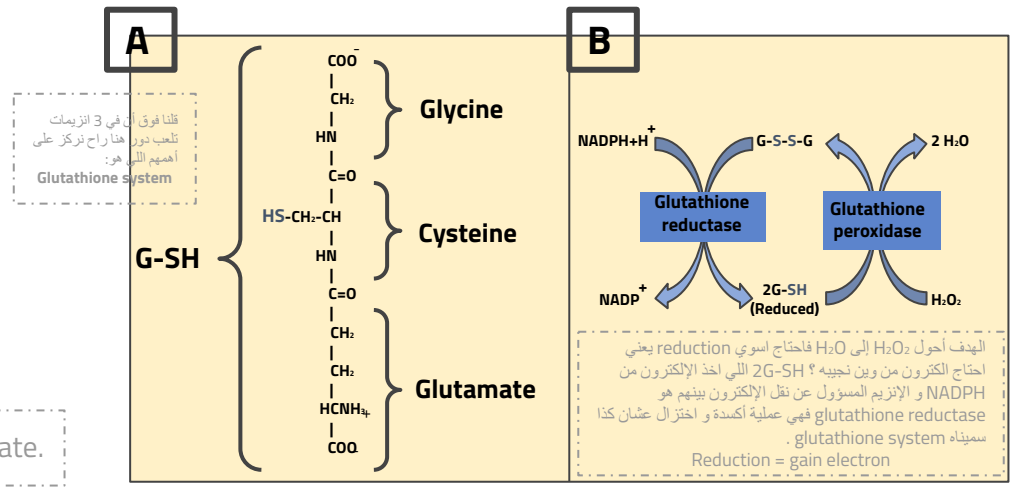
Effects of ROS



Glutathione system

- Present in most cells.
- Chemically detoxifies H₂O₂ (hydrogen peroxide) into water.
- Catalyzed by glutathione reductase.
- Uses NADPH that reduces glutathione which reduces H₂O₂.

Reduced glutathione (G-SH) consists of: glycine, cysteine, glutamate.



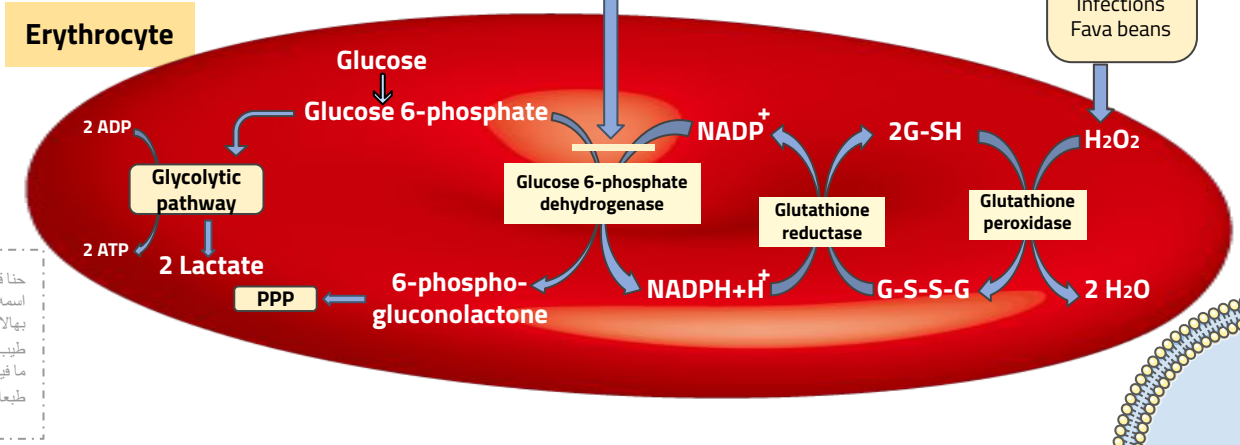
G6PD deficiency

- Leads to NADPH deficiency.
- Cells are unable to reduce free radicals.
- Oxidation of cellular proteins is increased causing impaired cell functions.

Glucose 6-phosphate dehydrogenase deficiency impairs the ability of an erythrocyte to form NADPH, resulting in hemolysis.

Oxidant stress

Certain drugs
Infections
Fava beans



حنا قلنا فوق أهمية NADPH وكيف يؤثر على العملية طيب وش المشكلة هنا ؟ ال NADPH يجي من انزيم اسمه Glucose 6-phosphate dehydrogenase زي ما هو واضح بالصورة طيب اللي عندهم خلل بهالانزيم deficiency = No NADPH والعملية كلها ما راح تصير ويزيد Radicle وتموت الخلية. طيب ليش خصصنا بس RBCs ما قلنا باقي الخلايا رغم أن النقص على كل أنواع الخلايا؟ باختصار في RBCs ما فيه مصدر ل NADPH غير هالمصدر لأنه ما يصنع طاقة عكس باقي الخلايا اللي عندها مصادر أخرى. طبعاً ما عندها إلا هالمصدر ليش؟ Because it does not have a nucleus



Nitric Oxide (NO)

1

Endothelial-derived relaxing factor (EDRF).

2

Causes **vasodilation** by relaxing vascular smooth muscle

3

Is a **gas** with short half-life (3-10 sec).

- SHORT HALF LIFE = FAST EFFECT.
- The short half life indicates fast effect of NO

4

NO + Oxygen/Superoxide \rightarrow Nitrates, Nitrites, **Peroxynitrite** ($O=NOO^-$).

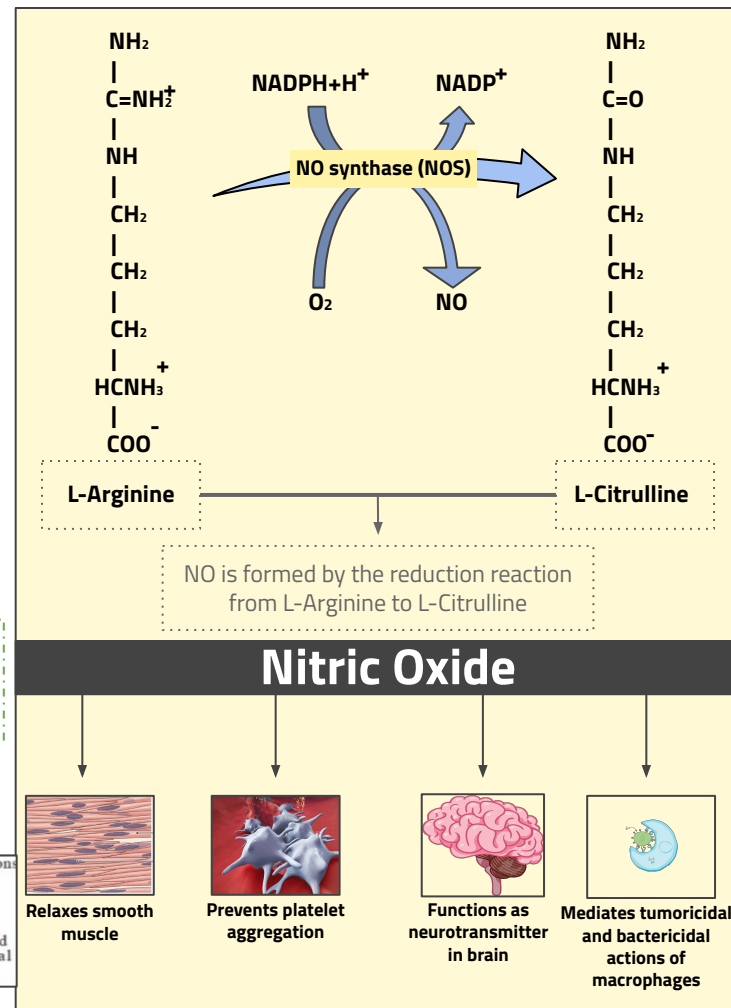
5

Peroxynitrite is a Reactive Nitrogen Species (RNS).




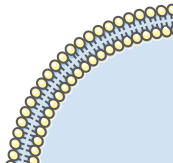
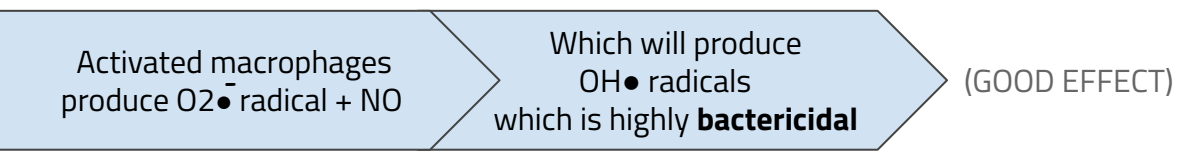
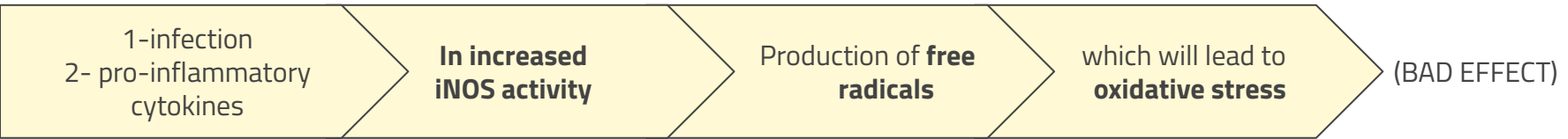
الثلاث أنواع
وخصوصا
Peroxynitrite
لها آثار سلبية زي
آثار NO

Synthesis and some of the actions of nitric oxide (NO). NADPH = reduced nicotinamide adenine dinucleotide phosphate. [Note: Flavin mononucleotide, heme, and tetrahydrobiopterin are additional coenzymes required by NOS.]



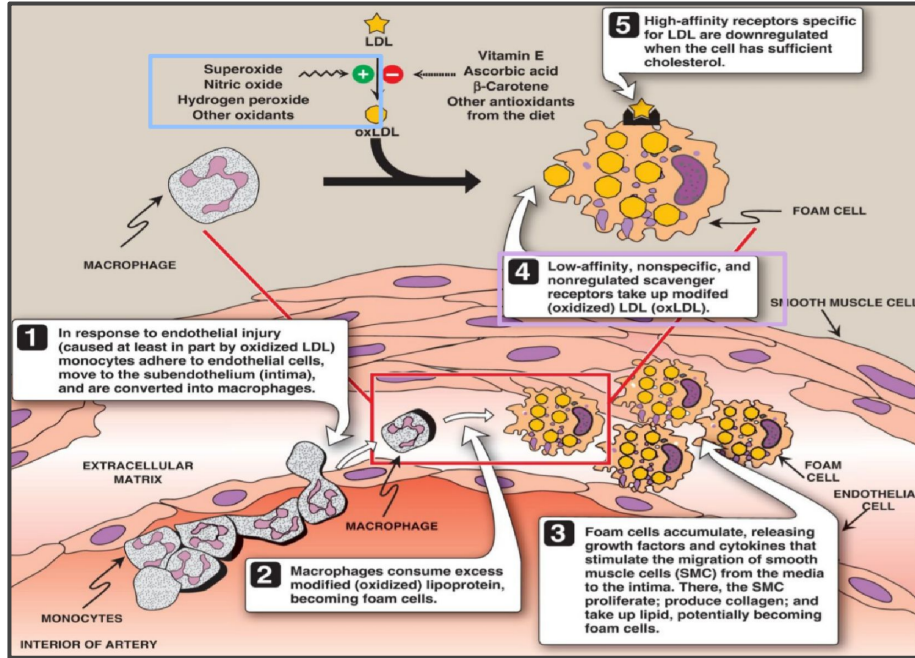
Nitric oxide synthase

<p>تميزه لك يا راعي الكورة تستاهل BEIN</p> 	eNOS	nNOS	iNOS	bNOS
Location	<u>E</u> ndothelium	<u>N</u> eural tissue	Macrophage, Neutrophils	<u>B</u> acteria
Function <small>All functions are Normal لكن بحد معين</small>	Vaso-relaxation <small>It is present all the time</small>	Neurotransmission	iNOS activity (normally low) increased by : - Infection. - Pro-inflammatory cytokines.	-



Oxidative Stress And Atherosclerosis

Animation



From 437

1. Superoxide, nitric oxide, hydrogen peroxide, or any other oxidant oxidize LDL to oxLDL
2. oxLDL binds to scavenger receptors "on the surface of macrophages"
 - ☆ Unlike the LDL receptor, the scavenger receptor is not downregulated in response to increased intracellular cholesterol.
3. Cholesteryl esters accumulate in macrophages and cause their transformation into "foam" cells
4. "foam" cells participate in the formation of atherosclerotic plaque



موفقين يا دكاترة المستقبل
ولا تنسون فعالية كل يوم



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.

Summary



Click [HERE](#)

Or

Scan the code for the
amazing summary



Quiz

Q1: Which of the following is an antioxidant Enzyme ?

- A/ Vitamin C
- B/ Glutathione System
- C/ Vitamin A
- D/ Beta-Carotene

Q2: Which of the following is Non-free radical source of ROS?

- A/ Superoxide
- B/ Hydroxyl radical
- C/ Hydrogen peroxide
- D/ All of the above

Q3: Which of the following is a disease due to oxidative stress?

- A/ Obesity
- B/ Cancer
- C/ Rheumatoid arthritis
- D/ All of the above

Q: What happens if there is cellular imbalance of oxidants and antioxidants ?
Damage of DNA, protein and lipids

Q4: What's the amino acid required for NO synthesis ?

- A/ L-Arginine
- B/ D-Arginine
- C/ L-Citrulline
- D/ D-Citrulline

Q5: Which of the following is not an effect of ROS?

- A/ DNA damage
- B/ RNA damage
- C/ Protein denature
- D/ Chemotaxis

Q6: Which of the following is the function of iNOS ?

- A/ Neurotransmission
- B/ Produce ROS
- C/ Vasodilation
- D/ Infection

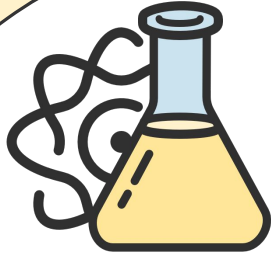
Q: Mention 3 effects of ROS?

Slide 6

Q: What are the 4 types of NOS ?

Mnemonic: **BEIN** sport
- bNOS
- eNOS
- iNOS
- nNOS

Special Thanks to Aisha Alhamed for her EXTRAORDINARY efforts!



Biochemistry 441

Girls

★ **Leader:** Wareef Almousa

Fay Alluhaidan
Manal Aldhirgham
Fatimah Albenmousa

Haya Alshalooob
Maram Alenzi
Futoon Almotairi

Organizer: Aisha Alhamed

Boys

★ **Leader:** Abdulrahman Alroqi

★ **Sub-leader:** Hamad Aljubayr

Anas Alharbi
Rayan Alahmari
Mohammed Aloufi

Faisal Alazmi
Abdulrahman Badghaish
Ali Almatri

Reviser: Mohannad Mallat

Organizer: Abdullah Alqarni

Special Thanks to Arwa Almobeirek for the Great Theme!



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