بسم الله الرحمـٰن الرحيم

(وَفَوْقَ كُلِّ ذِي عِلْمٍ عَلِيمٌ)

Metabolism | FINAL 4

PPP pt.2

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NST

Reviewed by : NST

وَلِلَّهِ الْأَسْمَاءُ الْحُسْنَى فَادْعُوهُ بِهَا

المعنى: الذي أحاط علمه بالأمور الدقيقة، والذي يوصل رحمته وخيره إلى عباده بالطرق الخفية.

الورود: ورد في القرآن (٧) مرات.

الشاهد: ﴿ وَهُوَ ٱللَّطِيفُ ٱلْخَبِيرُ ﴾ [الأنعام:١٠٣].

٤١

اضغط هنا لشرحٍ أكثر تفصيلًا

❑ Sources of ROS in the cell

- Oxidases:

  e- + O2

  - ✓ Most oxidases produce H2O2 (peroxidase) Superoxide also
  - ✓ Oxidases are confined to sites equipped with protective enzymes

- Oxygenases:

- Mono oxygenases (hydroxylases), they incorporate one Oxygen atom into the substrate while the other oxygen atom becomes reduced to water.
- Dioxygenases in the synthesis of prostaglandins, thromboxanes, leukotrienes, they incorporate complete molecular oxygen O2 into the substrate.
- Coenzyme Q in Respiratory chain
- Respiratory Burst (during phagocytosis) O2 -, OH ● , NO, HOCl, H2O2
- Ionizing Radiation OH● By X-Ray or UV, etc...

❑ Cytochrome P450 Mono-oxygenase

- Mixed function oxygenase
- Super family of structurally related enzymes

➢ **Cytochrome P450 is found in 2 systems:**

I. Mitochondrial system:

✓ **Used for** Synthesis by hydroxylation of steroids, cholesterol , bile acids, active form of Vit. D

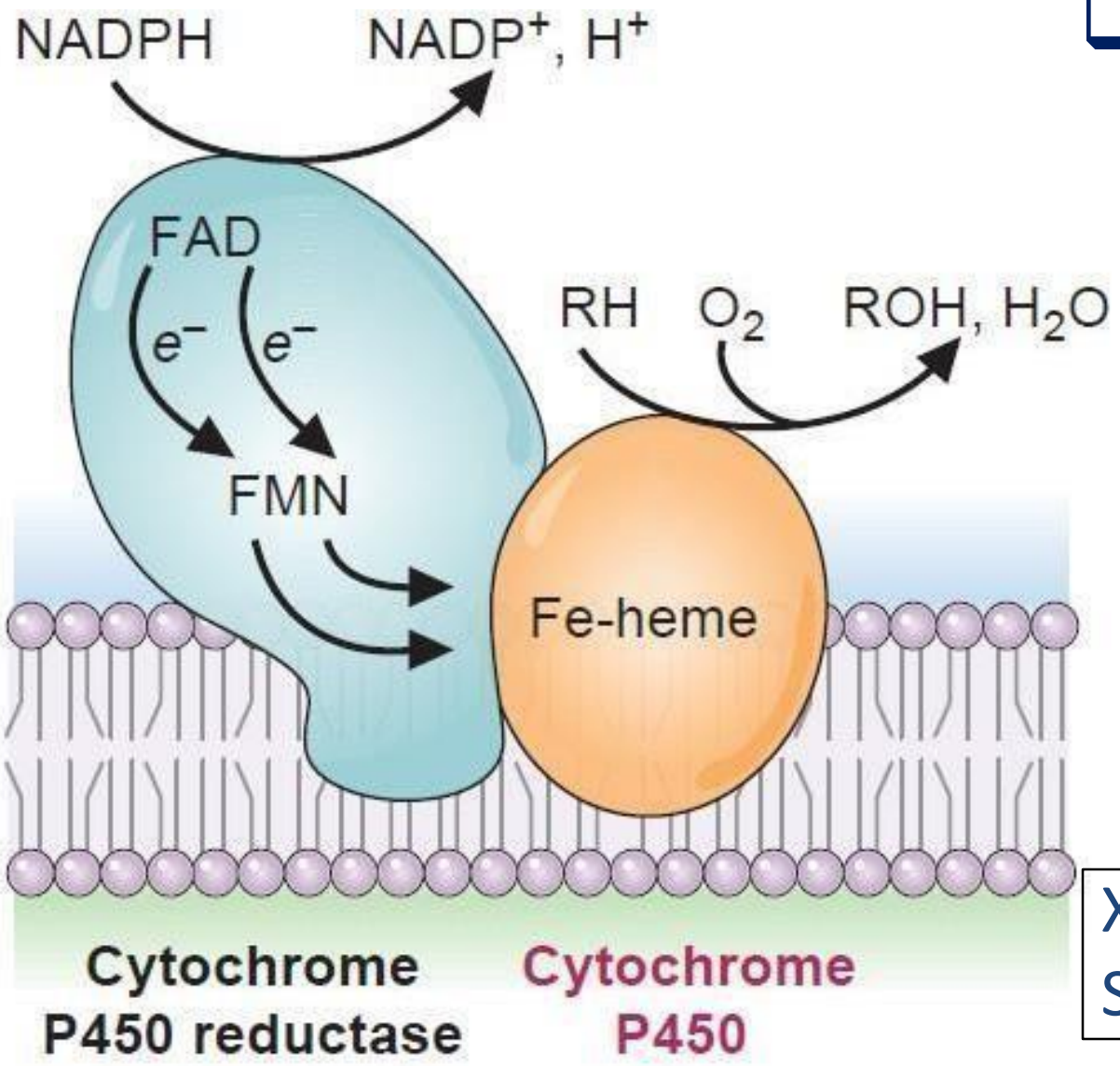
II. Microsomal system

✓ Detoxification of foreign compounds

✓ Activation or inactivation of Drugs

✓ Solublization to facilitate excretion in urine or feces

❑ Cytochrome P450 Mono-oxygenase



Accidental release of free radical intermediates may occur

XH2: electron donor
S: substrate

$$O_2 + S + XH_2 \longrightarrow H_2O + SOH + X$$

The substrate and NADPH is oxidized, O2 is reduced to water.

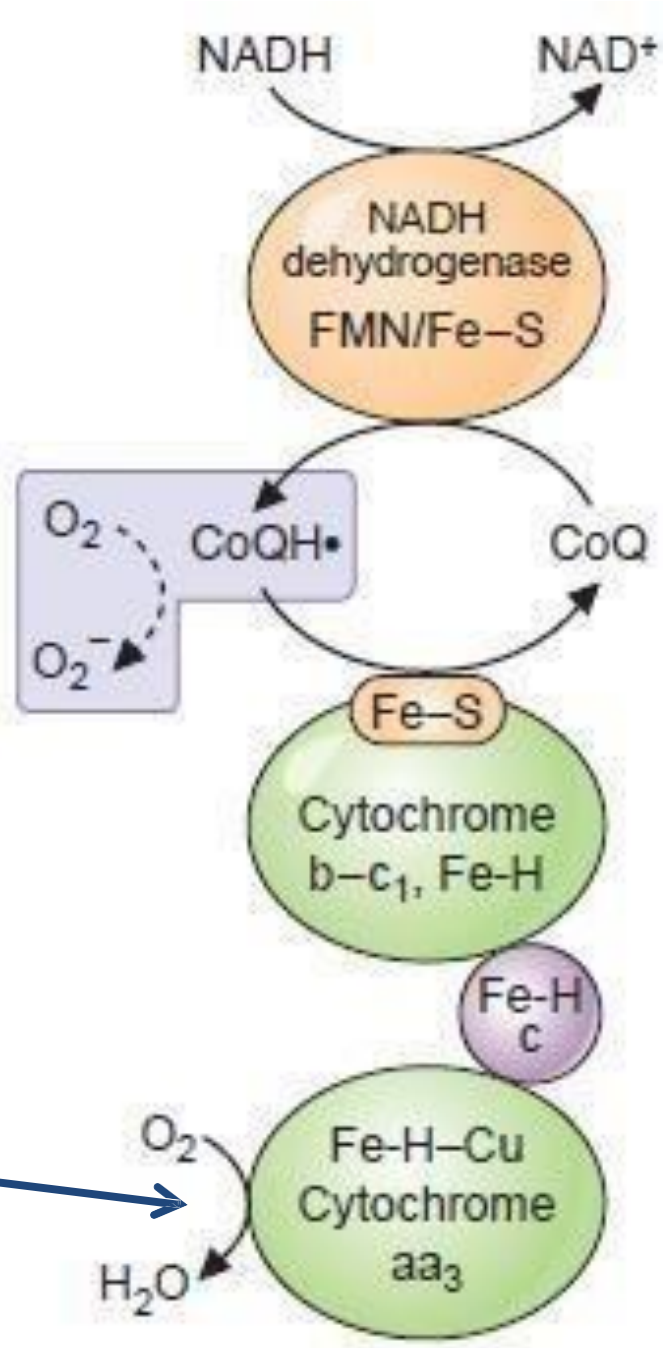
❑ Generation of O_2^- by the respiratory chain

- Ubiquinone is also considered a source for ROS

Accidental non-specific interaction

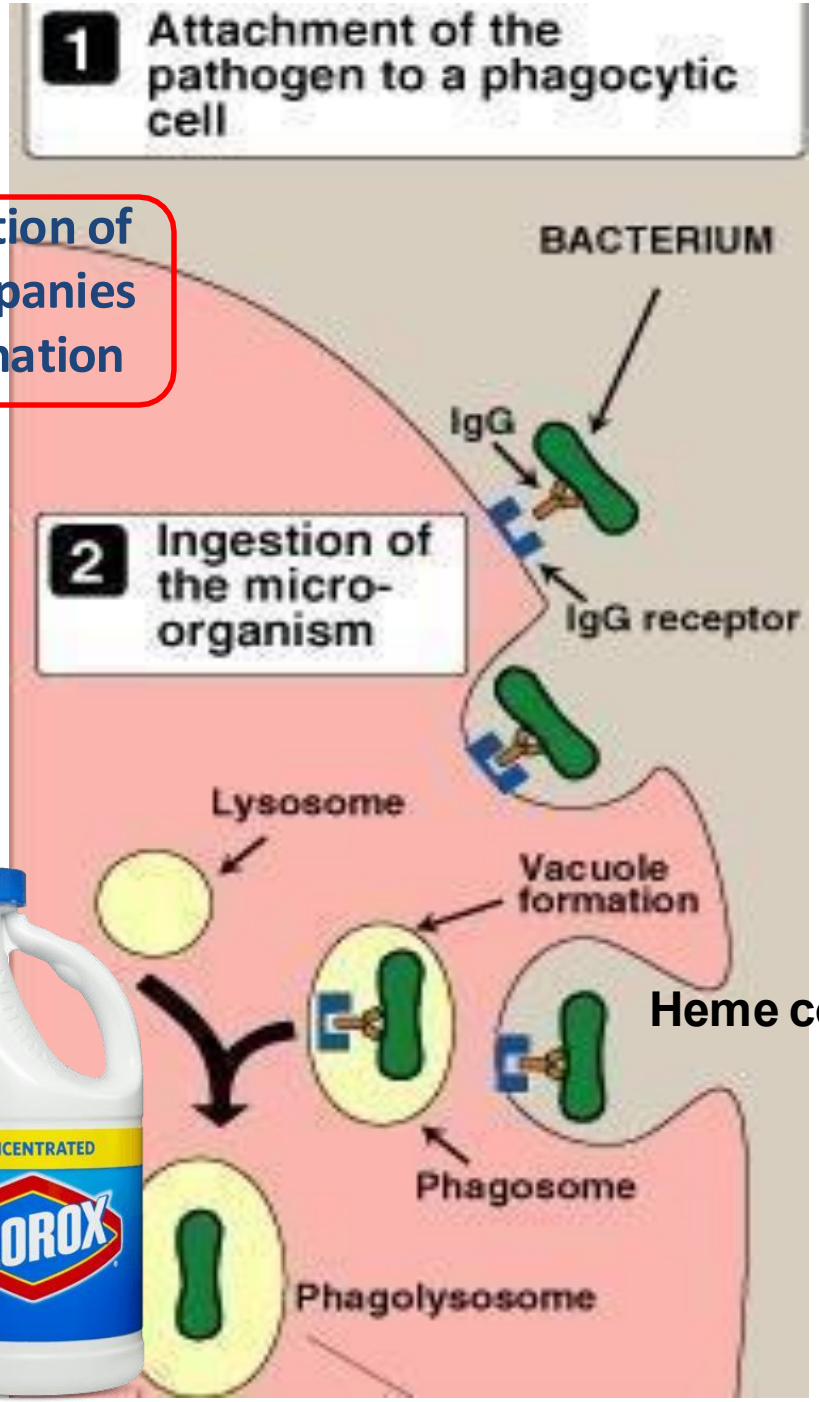
Major source of free radicals

Binuclear center prevents release of free O_2 radicals.

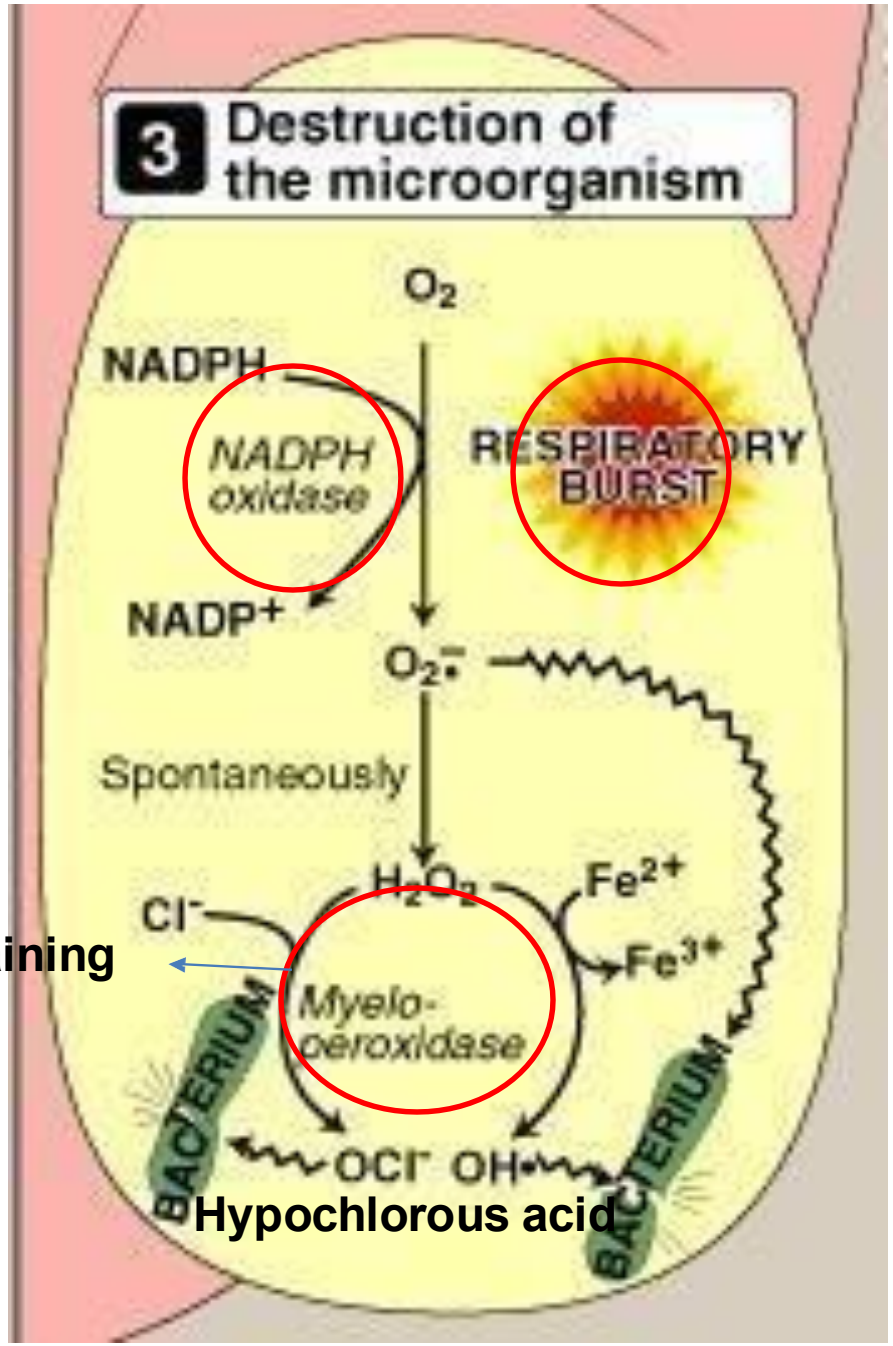


Rapid consumption of O_2 that accompanies superoxide formation

Phagocytosis is the oxygen-dependent pathway of microbial killing by phagocytes.



Heme containing



H2O2 can also be reduced to water by catalase or glutathione peroxidase

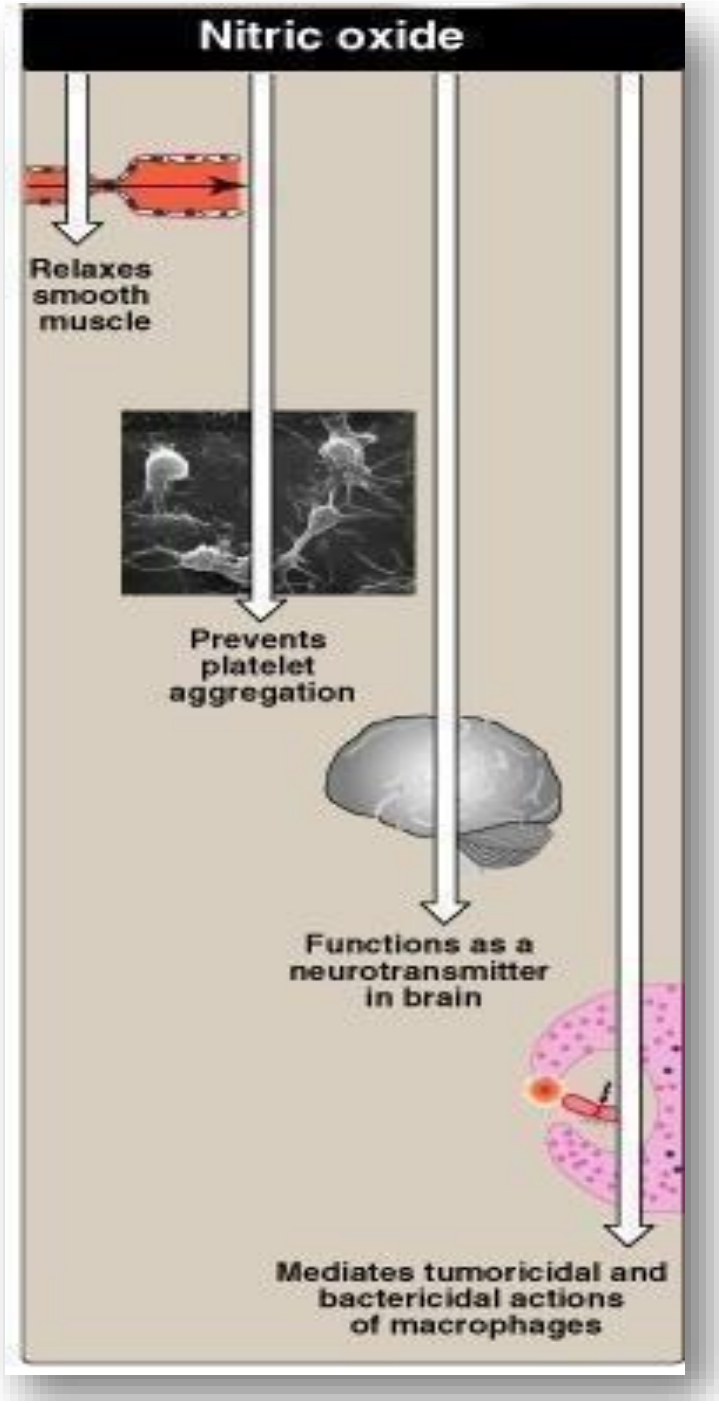
❑ The respiratory burst in phagocytes

- **Respiratory burst** is the rapid consumption of O2 that accompanies superoxide formation.
- **Phagocytosis** is the oxygen-dependent pathway of microbial killing by phagocytes.

➢ The microbe must attach at specific phagocytic receptors (IgG receptors) on the cell surface and then be internalized or endocytosed into the inside forming phagosome, the latter fuses with the lysosomes giving phagolysosome. Now molecular oxygen O2 will be reduced to superoxide, oxidizing NADPH into NADP+ by the activity of **NADPH oxidase** enzyme. Superoxide can be, spontaneously or by **superoxide dismutase enzyme**, converted into H2O2, both can act on the microbe. H2O2 Can be further converted into hydroxyl radical, oxidizing Fe+2 to Fe+3, or into hypochlorite by the activity of **myeloperoxidase enzyme** (heme-containing emzyme).

❑ NO and Reactive Nitrogen Oxygen Species (RNOS)

- Nitric Oxide is the father molecule of RNOS.
- It is an endogenous gaseous signaling molecule that can diffuse readily/passively, exerting its effect locally
- Essential for life and toxic
- It acts as a Neurotransmitter , and a vasodilator
- It reduces ↓Platelet aggregation
- At high concentration combines with $O_2\bullet^-$ or O_2 to form **RNOS**
- **RNOS** are involved in neurodegenerative diseases (like Parkinson's, Alzheimer's) and inflammatory diseases



❑ NO Synthesis

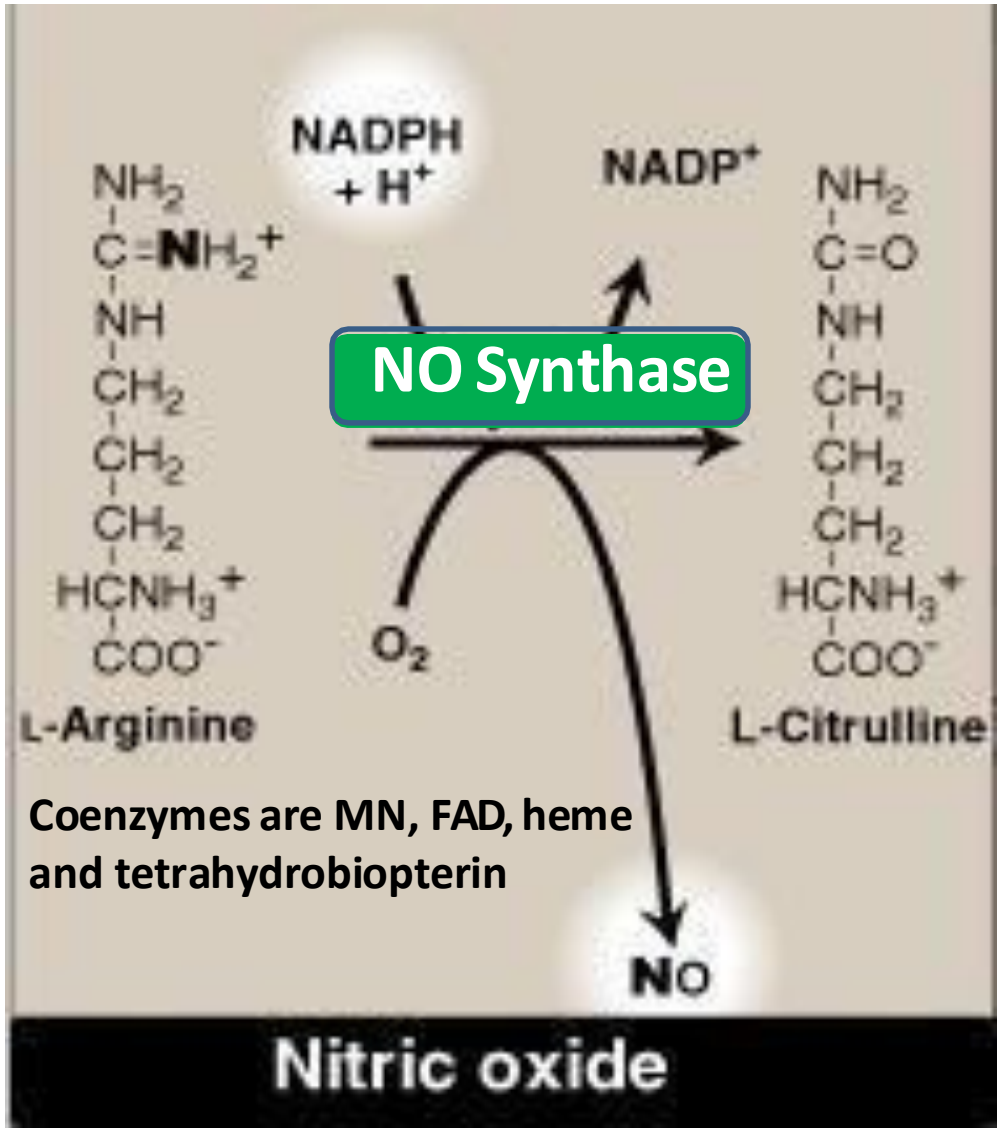
- It is done by the enzyme NO Synthase, which has three isoforms:

I. nNOS, found in neural cells

II. eNOS, found in endothelial cells
   - ✓ Both are constitutive, meaning that they are always expressed and synthesized without the need for a stimuli

III. iNOS, which is inducible, meaning its synthesis can be activated by stimulants like infection in Ca+2 independent manner.

- Induction of transcription in many cells of immune system➔↑↑ NO ➔ RNOS to kill invading bacteria



❑ Action of NO on vascular endothelium

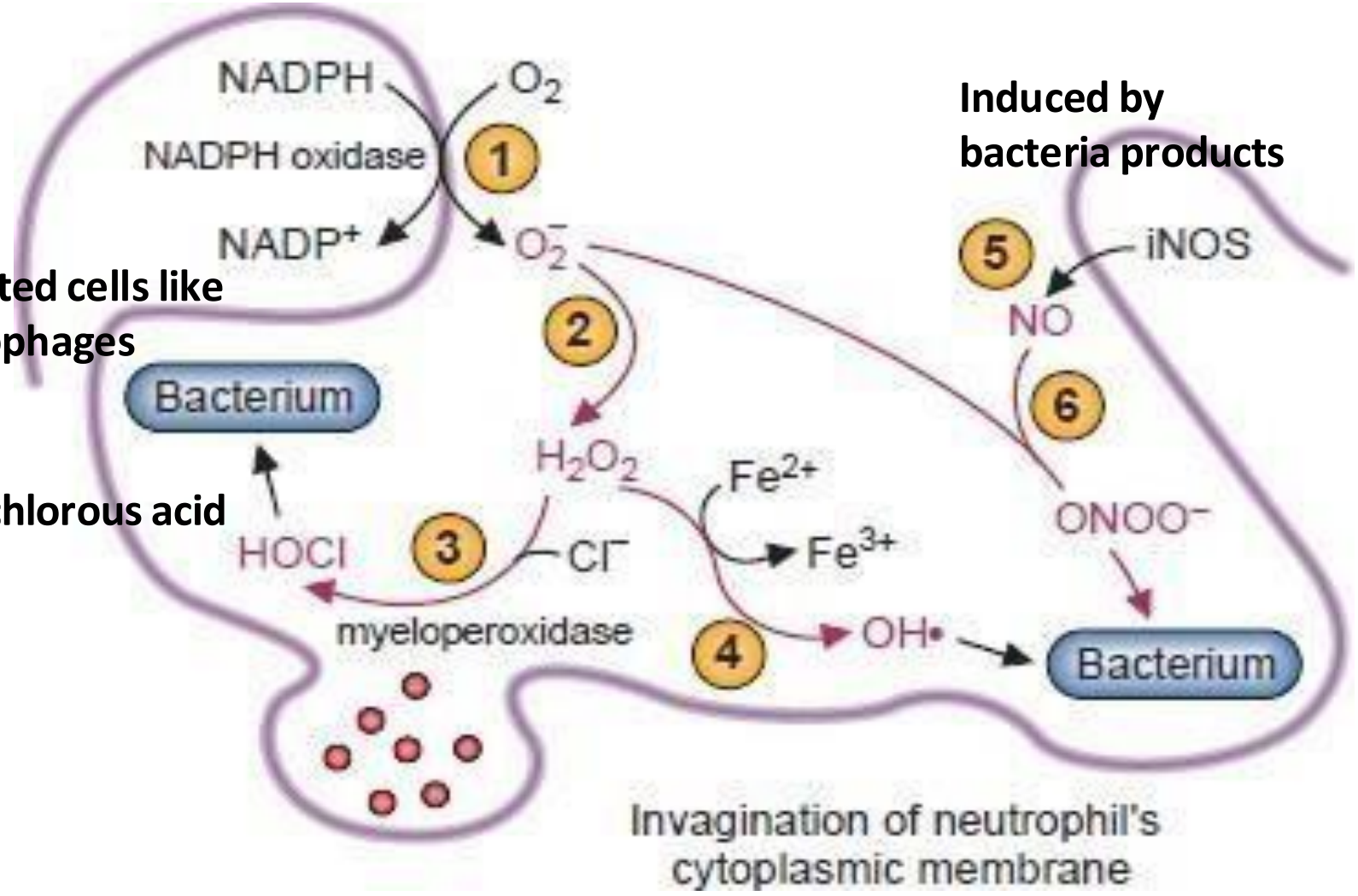
Synthesis by endothelia cells → smooth muscle

- NO diffuses into the smooth muscle activating **guanylyl cyclase** producing cGMP from GTP, cGMP activates **protein kinase G**, which in turn phosphorylates Ca+2 channels ,inhibiting their entry into smooth myocytes inducing relaxation.

❑ NO role during bacterial infections

Activated cells like macrophages

Hypochlorous acid



NO is synthesized by iNOS, which diffuses through phagolysosomal membrane reacting with superoxide to produce RNOS (ONOO-) which furthermore aids in bacterial killing.

❑Test your knowledge:

What are the differences between NADPH and NADH in terms of their roles in the cell? Q.1

A. NADPH is used for energy production, while NADH is for biosynthesis.

B. NADPH is primarily used in the Krebs cycle, while NADH is used in the electron transport chain.

C. NADPH is for biosynthesis; NADH is for energy production.

D. NADPH is found in the mitochondria, while NADH is in the cytosol.

What is the relationship between NADPH and reactive oxygen species (ROS)? Q.2

A. NADPH promotes the formation of reactive oxygen species.

B. NADPH has no relationship with reactive oxygen species.

C. NADPH is converted to NADH in the presence of ROS.

D. NADPH reduces reactive oxygen species, preventing damage.

What is the impact of oxidative stress on red blood cells? Q.3

A. It leads to increased production of hemoglobin, improving oxygen transport.

B. It promotes the regeneration of antioxidants, protecting red blood cells.

C. It enhances the flexibility of red blood cells, allowing better circulation.

D. It causes protein denaturation and hemolysis in red blood cells.

What are the main products generated by the oxidative phase of the PPP?

Q.4

A. Ribose-5-phosphate and CO2

B. ATP and NADH

C. NADH and CO2

D. NADPH and CO2

What role does NADPH play in maintaining glutathione in red blood cells?

Q.5

A. NADPH is involved in the synthesis of hemoglobin in red blood cells

B. NADPH helps in the formation of reactive oxygen species (ROS)

C. NADPH reduces oxidized glutathione (G-S-S-G) to GSH

D. NADPH is used to synthesize ATP in red blood cells

A 30-year-old woman presents with fatigue and jaundice. Blood tests reveal hemolytic anemia and elevated levels of oxidative stress markers. She has a history of consuming fava beans and is concerned about her health.

Q.6

What is the primary metabolic pathway affected in this patient?

A. Glycolysis is unaffected

B. Beta-oxidation is not involved

C. Krebs cycle remains intact

D. Pentose phosphate pathway is impaired

A 30-year-old man of Mediterranean descent presents with sudden fatigue, pallor, and dark urine after consuming fava beans during a family gathering. He reports a history of similar episodes triggered by certain medications.

Q.7

What is the most likely cause of his symptoms?

A. Thalassemia

B. Sickle Cell Anemia

C. G6PD Deficiency

D. Iron Deficiency Anemia

What is the significance of the ratio of NADP+/NADPH in hepatocytes?

Q.8

A. It reflects the energy status of the hepatocyte.

B. It influences the synthesis of ATP in the mitochondria.

C. It indicates the level of oxidative stress in the cell.

D. It supports biosynthesis and detoxification processes.

Which tissues primarily utilize NADPH for fatty acid biosynthesis?

Q.9

A. Brain tissue

B. Muscle tissue

C. Kidney tissue

D. Liver, adipose tissue, lactating mammary glands

How does G6PD deficiency provide resistance to malaria?

Q11

A. It increases oxidative stress, impairing malaria survival.

B. It leads to increased levels of hemoglobin, which is toxic to malaria.

C. It enhances the immune response against malaria parasites.

D. It increases the production of red blood cells, reducing parasite load.

A 30-year-old woman is undergoing treatment for a chronic inflammatory disease. Her physician notes that her red blood cells are struggling to maintain reduced glutathione levels, which could lead to oxidative stress. The doctor discusses the role of NADPH in protecting against reactive oxygen species.

Q.13

How does NADPH contribute to maintaining red blood cell health?

A. It directly reduces hydrogen peroxide into water.

B. It converts NADH to NAD+ for energy production.

C. It helps keep glutathione in its reduced form.

D. It increases the production of superoxide radicals.

How does nitric oxide synthase contribute to the production of nitric oxide?

Q.10

A. Nitric oxide synthase converts L-arginine to nitric oxide using coenzymes.

B. Nitric oxide synthase breaks down nitric oxide into reactive nitrogen species.

C. Nitric oxide synthase converts L-citrulline to nitric oxide using oxygen.

D. Nitric oxide synthase synthesizes nitric oxide from glucose and regulates blood sugar levels.

What is the importance of the respiratory burst in phagocytic cells?

Q.12

A. It helps in the attachment of pathogens to phagocytic cells.

B. It reduces inflammation during the immune response.

C. It promotes the production of antibodies against pathogens.

D. It generates reactive oxygen species to kill pathogens.

How does the structure of glutathione contribute to its function as an antioxidant?

Q.14

A. Glutathione's structure allows it to bind to metal ions, enhancing its antioxidant capacity.

B. The tripeptide structure of glutathione prevents it from being oxidized easily, making it a stable antioxidant.

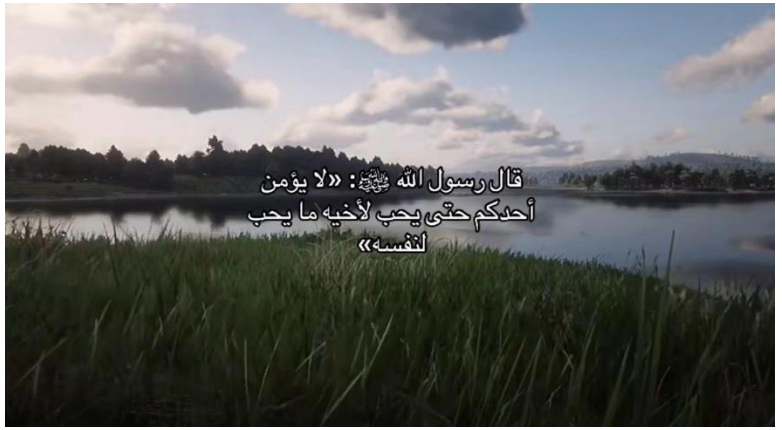
C. Glutathione's amino acid composition allows it to form stable complexes with free radicals, neutralizing them.

D. The thiol group in cysteine allows glutathione to act as a reducing agent.

Answers:

1. C
2. D
3. D
4. D
5. C
6. D
7. C
8. D/C
9. D
10. A
11. A
12. D
13. C
14. D

رسالة من الفريق العلمي:



- والذي نفسُ مُحَمَّدٍ بيدِهِ لا يُؤْمِنُ أحدُكُم حتى يُحِبَّ لِأَخِيهِ ما يُحِبُّ لنفسِهِ من الخيرِ

خلاصة حكم المحدث : صحيح

الراوي : أنس بن مالك | المحدث : الألباني | المصدر : صحيح النسائي | الصفحة أو الرقم : 5032

يُبيِّنُ النبيُّ صلَّى اللهُ عليه وسلَّمَ في هذا الحديثِ الجليلِ -الذي قِيلَ فيه: إنَّه رُبُعُ الإسلامِ، ومِن أحاديثَ أربعةٍ تَتفرَّعَ عنها جِماعُ آدابِ الخيرِ- أنَّه **لا يَتحقَّقُ الإيمانُ الكامِل** لأحدٍ مِن المُسلِمينَ -والنفيُ هنا لا يُقصَدُ به نفْيُ أصلِ الإيمانِ، وإنَّما نفْيُ الكَمالِ- حتَّى يُحِبَّ لأخيهِ ما يُحِبُّ لنفْسِه مِن الطَّاعاتِ وأنواعِ الخَيراتِ في الدِّينِ والدُّنيا، ويَكرَهَ له ما يَكرَهُ لنفْسِه، فإنْ رَأى في أخيه المسلِمِ نَقْصًا في دِينِه، **اجتهَدَ في إصلاحِه**، وإنْ رأى فيه خيرًا **سدَّدَه وأعانَه** على الثباتِ عليه والزِّيادةِ منه؛ فلا يكونُ المؤمنُ مُؤمنًا حقًّا حتَّى يَرضَى للنَّاسِ ما يَرضاهُ لنفْسِه، وهذا إنَّما **يَأتي مِن كَمالِ سَلامةِ الصَّدرِ** مِن الغِلِّ والغِشِّ والحسَدِ؛ فإنَّ الحسَدَ يَقتضي أنْ يَكرَهَ الحاسدُ أن يَفُوقَه أحدٌ في خَيرٍ، أو يُساويَه فيه؛ لأنَّه يُحِبُّ أنْ يَمتازَ على النَّاسِ بفَضائلِه، ويَنفرِدَ بها عنْهم، **والإيمانُ يَقْتضي خِلافَ ذلك**، وهو أنْ يَشرَكَه المؤمنون كلُّهم فيما أعطاهُ اللهُ مِن الخَيرِ.

For any feedback, scan the code or click on it.

Corrections from previous versions:

Versions	Slide # and Place of Error	Before Correction	After Correction
V0 → V1			
V1 → V2			