The Physiology of Hyperbaric Oxygen Therapy

Free Radicals and Reactive Oxygen Species

I. Introduction – Definition, Source, function and Purpose

A. Definition of free radicals and **r**eactive **o**xygen **s**pecies (ROS).

1. Reactive oxygen species (ROS) are highly reactive ions and "free radicals" (chemicals containing atoms with an unpaired electron in its outer orbit) involving oxygen molecules.
2. "Free radicals" are present that do not contain oxygen, but ROS refers to free radicals containing oxygen molecules.
3. Characteristics:

    a. Short lived
    b. Unstable
    c. React with other molecules to achieve stability

B. Source of ROS's

1. Byproduct of cellular respiration (presence of redox cycling compounds).
2. Synthesized by enzyme systems – phagocytic cells, neutrophils and macrophage (NADPH oxidase, myeloperoxidases).
3. Exposure to ionizing radiation
4. Smoking, herbicides, pesticides, fried foods, etc.
5. Production:

    a. Chain reaction, a free radical steals an electron from a nearby compound forming a new free radical. Free radicals may steal electrons from cellular structures or molecules.
    b. By normal cellular respiration – electron transport system – often oxygen is the terminal electron acceptor in the cell mitochondria → ROS
    c. Figure on production of common free radical species.

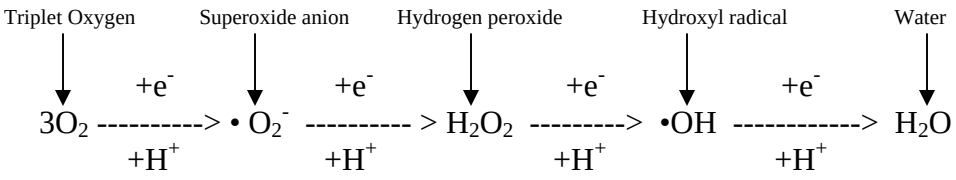
C. Function and purpose

1. Necessary for production of some hormones (thyroxine).
2. Generated to kill some types of bacteria and engulfed pathogens.
3. Normal cell functions and cell signaling.
4. A balance:

    a. Free radicals generated by normal processes do become harmful if inadequate anti-oxidant defenses are present. A balance between production and removal/inactivation is required.
    b. When free radicals are present in excess of the defense mechanism's ability to control them is when damage may occur.
    c. Anti-oxidants – compounds which will provide electrons to free radicals to neutralize them. The compounds are able to accommodate the loss of an electron without becoming reactive.
    d. Anti-oxidants: Vitamin E, SOD, catalase, glutathione peroxidase, Vitamin C, beta-carotene, coenzyme Q.

D. Free radicals in disease. Excessive free radical production has been involved in the occurrence in several disease processes.

1. drug toxicities
2. inflammation
3. aging
4. fibrosis
5. carcinogenesis
6. lipid peroxidation cellular membranes
7. implicated in several specific diseases
    a. atherosclerosis
    b. degenerative neurologic disease
    c. reperfusion injury
8. oxygen toxicity



II. Reactive Oxygen Species

A. Individual species

1. Superoxide anion
    a. $\bullet O_2^-$
2. Hydroxyl radical
    a. $\bullet OH$
3. Hydrogen peroxide
    a. H_2O_2
4. Nitric oxide
    a. $\bullet NO$
5. Hypochlorite ion
    a. OCl^-
6. Ozone
    a. O_3
7. Thiyl radicals
    a. $RS\bullet$
8. Carbon centered radicals
    a. $\bullet O_2CCl_3$

III. HBOT and ROS's

A. ROS affects depend on;

1. balance with anti-oxidant production
2. physical condition of the patient
3. concentration, frequency and duration of hyperbaric oxygen exposure.

B. Exposure limits

1. 2.5 ATA and less → no significant increase in ROS production.
2. Frequency and duration of treatment that might significantly increase ROS production in horses is not known.
    a. The limits of accumulative or acute exposure to hyperbaric oxygen have not be established.

C. HBOT and benefits of ROS production

1. Enhancement of antimicrobial effects of cellular immunity especially in hypoxic environments.
2. Some evidence exists that indicating that HBOT may actually decrease lipid peroxidation in cell membranes.

IV. Facts about free radicals, ROS, and hyperbaric oxygen therapy.

A. Hyperbaric oxygen therapy using pressures at or less than 2.5 ATA do not significantly increase ROS in the presence of normal anti-oxidant defenses.
B. The detrimental effects of ROS is seen when there is an imbalance between ROS production and the bodies anti-oxidant production or availability.
C. ROS are generally a family of compounds that are short lived, unstable and highly reactive and will react with cellular molecules to achieve stability.
D. A certain amount of ROS are produced by normal cell respiratory functions through the electron transport system.
E. ROS and free radicals have an important role in the oxidative killing of micro-organisms.
F. A variety of anti-oxidants are either produced by the body or provided by dietary absorption for use in maintaining the balance between ROS and anti-oxidant defenses.

References

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Web Information

1. http://users.rcn.com/jkimball.ma.ultranet/BiologyPages/R/Introduction.html
2. http://www.exrx.net/Nutrition/Antioxidants/Introduction.html