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AUTHOR Janowiak, John J.
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ABSTRACT

This article presents a teaching methodology for free radical theory and discusses the role of antioxidants in human health. Free radicals are a normal byproduct of respiration, which allows the body to use oxygen, liberate energy, and dispose of harmful substances. The body's antioxidants and nutritional antioxidants quench most of the free radicals produced. Free radicals drain the body's molecular system of energy by stealing energy in the form of electrons, a process which manifests itself in aging. Growing evidence indicates that this process can be prevented or delayed by dietary changes, such as reduction in fat intake and increased consumption of fruits, grains, and vegetables as well as increased intake of dietary antioxidants, such as vitamin E. Teaching about antioxidant nutrients can be enhanced by renting a cartoon video with a scene from the television cartoon "Mighty Mouse" and showing the class a scene where Mighty Mouse transforms into a super-mouse by consuming nutrients/vitamins and asking appropriate questions. Other effective teaching techniques include showing a transparency on the levels of organization in nature or on a simplified model of atomic structure; explaining the dangers of free radicals to students; asking students to list the fruits and vegetables recently consumed and focusing on including more of these in their diet; and explaining the benefits of eating fresh fruits and vegetables to students. (Contains 21 references.) (CK)

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Teaching Methods in Nutrition: Free Radicals, Antioxidants, and Human Disease

* John J. Janowiak, Ph.D.
Associate Professor; Health Education
Department of Curriculum and Instruction
Appalachian State University
Boone, North Carolina 28608

* Corresponding Author

Teaching Methods in Nutrition: Free Radicals, Antioxidants, and Human Disease

Abstract

Over the last decade, two unlikely terms have migrated from the chemistry lab to popular culture: free radicals and antioxidants. Magazine advertisements and television commercials regularly make reference to how free radicals age the body and contribute to human disease. Common literature also extols the preventive benefits of antioxidant nutrients. This article will present a teaching methodology for free radical theory and discuss the role of antioxidants in human health.

Teaching Methods in Nutrition: Free Radicals, Antioxidants, and Human Disease

"Aging and death do seem to be what nature has planned for us.
But what if we have other plans?"

- Bernard Strehler, biological gerontologist

Introduction

"Free radicals are implicated in Parkinson's disease"; "taking vitamin E capsules will prevent heart attacks"; "our anti-aging cream contains free radical scavengers." Advertisements and research announcements such as these demonstrate the growing interest in free radicals and antioxidants. In a recent cartoon in the *The New Yorker*, a diner asks a waitress, "What do you have that's rich in antioxidants?". None-the-less, the medical community has taken free radical theory very seriously since it's conception by Denham Harman, M.D., Ph.D., currently professor emeritus at the University of Nebraska at Omaha. In the early 1950's Harman was employed as a chemist at Shell Development Company's Research Division investigating free radicals. After completing medical school Harman joined Donner Laboratory at the University of California at Berkeley, where he studied the effects of radiation on human disease. It was at the Donner Laboratory that Harman connected radiation exposure to induced mutations, cancer and accelerated aging - whose effects were conjoined with oxygen free radicals. He was convinced that the oxidative process occurring within living cells, by which the chemical energy of organic molecules is released in a series of metabolic steps involving the consumption of oxygen and the liberation of carbon dioxide and water, also generated free radicals. In July, 1955, while at the University of California, Harman published a remarkably lucid scientific paper titled; "Aging: A Theory Based on Free Radical and Radiation Chemistry" (Challem, 1995).

At the time Harmon subsumed that his theory could not be directly proven so he began experiments that suggested free radicals were a factor in heart disease, cancer and aging. In an early study Harman demonstrated that the life span of mice could be extended by a diet (i.e. using the amino acid cysteine) that protected against radiation-induced free radicals (Harmon, 1957). Simultaneously, Harman proposed that oxidation of the low-density lipoprotein form of cholesterol was a key factor initiating heart disease. In 1964 Harman discovered free radicals in human blood and demonstrated that antioxidants could extend life spans of experimental animals. In 1969 researchers discovered superoxide dismutase (SOD), a powerful antioxidant produced by the body, which established the foundation of the free radical theory (Challem, 1995).

Today, numerous confirming studies have established the role of free radicals in heart disease which is generally accepted by the medical community. Nearly 200 studies have shown that a high intake of antioxidants, from diet or supplements, reduce the risk of disease and extend life span. Among the recent findings are:

- The risk of developing cataracts can be significantly reduced through increased consumption of antioxidant nutrients (Taylor, 1993)
- Terminal cancer patients given large doses of vitamins C and E, beta carotene and other nutrients exceeded their life expectancy by 12 to 20 times (Hoffer, 1993).
- Beta carotene protects against radiation damage, according to a team of Japanese researchers who irradiated blood samples from college students (Umegake, 1994).
- High doses of vitamins A, B6. C. E and the mineral zinc reduce the rate of recurrent bladder cancer from 88 percent to 40 percent (Lamm, 1994).
- A large, diverse group of antioxidant nutrients - vitamins C, E, selenium, beta carotene and coenzyme Q10 - function synergistically and are more protective than a combination of vitamin E and selenium (Tappel, 1994).

What is a Free Radical?

Atoms contain a nucleus, and electrons move around the nucleus, usually in pairs. A free radical is an atom or molecule that contains one or more unpaired electrons (Halliwell, 1989). The unpaired electrons alter the chemical reactivity of an atom or molecule making it more reactive than the corresponding non-radical. The actual chemical reactivity of radicals varies quite a bit. The hydrogen radical H*, (the same as a hydrogen atom) contains 1 proton and 1 electron (therefore unpaired), and is the simplest free radical. Free-radical chain reactions are often initiated by removal of H* from other molecules (eg, during lipid peroxidation).

Free radicals are a normal byproduct of respiration, which allows the body to use oxygen, liberate energy, and dispose of harmful substances. Biochemists also describe the process as oxidation-reduction or redox. The body's antioxidants (SOD) and nutritional antioxidants quench most, but not all, of the free radicals produced. White blood cells (phagocytes) use free radicals to destroy bacteria and cells infected by viruses. The body makes a free radical called superoxide by adding one electron to the oxygen molecule. It is generally poorly reactive yet unavoidable. Activated phagocytes (neutrophils, monocytes, macrophages, eosinophils) generate large amounts of superoxide as part of the mechanism by which foreign organisms such as bacteria and viruses are killed (Babior, 1990). During chronic inflammations in the body this normal protective mechanism may become damaging. Free radicals, while simultaneously protecting the biological organism from disease, also damage DNA which slowly contributes to cancer and the aging process. About 1-3% of the oxygen we breathe in is used to make superoxide. Since humans consume a lot of oxygen, we may produce over 2 kg of superoxide in the body each year; individuals with chronic infections may make much more. Also, the liver's cytochrome P450 enzymes detoxify harmful chemicals while generating free radicals.

How do Free Radicals React?

When two free radicals meet, they may join their unpaired electrons and make a covalent bond (a shared pair of electrons). Thus superoxide and nitric oxide combine: $O_2 + NO \rightarrow ONOO^-$ (peroxynitrite). At physiological pH, peroxynitrite damages proteins directly, and decomposes into toxic products that include nitrogen dioxide gas, hydroxyl radical, and nitronium ion. Hence at least some of the toxicity of excess nitric oxide may involve its interaction with superoxide. In addition, superoxide can react with iron and copper ions, eventually to make a hydroxyl radical (Babior, 1990). However, most molecules in the body are not free radicals therefore any reactive free radical generated is likely to react with a non-radical. When a free radical reacts with a non-radical, a free-radical chain results and new radicals are formed. A simplified and useful way to understand this mechanism is that free radicals drain the body's molecular system of energy by stealing energy in the form of electrons. The electron energy that the free radicals steal is important for maintaining cell membrane structure. These electrons may be considered the molecular glue which holds all levels of biological structure together, from DNA and RNA to cell membranes. If one takes away the glue that holds the biological structure together, we get disorganization of cell function and cell replication, which manifests as increasing entropy and therefore aging. Attack of reactive radicals on membranes or lipoproteins starts the process of lipid peroxidation which is implicated in the development of atherosclerosis (Hertog, 1993).

Lipoproteins are any of a group of conjugated proteins in which at least one of the components is a lipid. Lipoproteins, classified according to their densities and chemical qualities, are the principal means by which lipids are transported in the blood. If hydroxyl radicals are generated close to DNA, they can attack the purine and pyrimidine bases and cause mutations. For example, guanine is converted into 8-hydroxyguanine and other products (Halliwell, 1989).

Antioxidants To The Rescue

Compounding the problem is the large numbers of free radicals generated by environmental factors such as ultraviolet radiation from sunlight, cigarette smoke, air pollution, alcohol consumption, excessive exercise, animal fats exposed to oxygen (such as ground hamburger), heating cooking oils to high temperatures, polyunsaturated fatty acids that have been chemically altered (such as hydrogenated oils found in potato chips and margarine, etc..). Uncontrolled, these free radicals can damage proteins, fats, and nucleic acids (DNA and RNA) in the body. We have control systems for free radicals mentioned earlier but these cannot control free radicals perfectly as long as we lead imperfect lifestyles. There is growing evidence that the major killers, cardiovascular disease and cancer, can be prevented or delayed to some extent by dietary changes, such as reduction in fat intake and increased consumption of fruits, grains, and vegetables (Block, 1992). When continuous free radical damage to DNA is not efficiently repaired the development of spontaneous cancers often occur. In cases such as these more dietary antioxidants may help. Increased dietary intakes of vitamin E have been shown to decrease death rates from myocardial infarction (Byers, 1993).

Antioxidants and Disease Prevention

Denham H rman, M.D. believes that antioxidant supplementation and consumption of antioxidant rich fruits, grains, and vegetables is vital in the face of oxidative stress. Harmon's own supplement regimen includes a daily intake of 200 mg vitamin E, 2,000 mg vitamin C, 100 mcg selenium and 30 mg coenzyme Q10 as well as 25,000 IU of beta carotene every other day. He has been tempted to take more, but has concerns that too many antioxidants might interfere with the normal redox process and cause fatigue (Challem, 1995). Epidemiological studies on serum antioxidants and diet suggest that an increased level of vitamin E and beta carotene reduces mortality from cancer in the lung and colon (Menkes, 1986; Blot, 1993). The cellular antioxidant defenses consist of multiple interdependent components of low and high molecular weight. A fine balance between several antioxidants appears to be more important for the overall protective capacity of the system than the activity of a single enzyme (Amstad, 1994). Also, in view of the multiple stages in carcinogenesis where antioxidants could act, it is to be expected that they are not anticarcinogenic in every case. While high antioxidant capacity shields DNA from oxidative damage and mutagenesis, it may at the same time protect "initiated" cells from excessive oxidant toxicity and apoptosis, and favor their clonal expansion in tumor promotion (Cerutti, 1991). None-the-less, since free radicals are able to cause genetic mutations, they have been implicated in the genesis of atherosclerotic plagues (a type of tumor) and cancer. Free radical quenchers such as vitamins C, E, selenium, and cysteine have been shown in experimental animals to prevent the development of some types of cancer. Peroxidized fats, the most common type of organic peroxide, are a source of free radicals (they also inhibit macrophages, white blood cells of the immune system, so that they do not attack and eat foreign invaders such as bacteria and cancer cells). Overweight individuals, who contain a larger amount of peroxidized fats in their body, are more likely to develop cancer and atherosclerosis than people of normal weight.

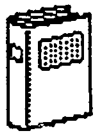
In conclusion, Dr. Harman, who developed the free radical theory of aging (1957), suggests three methods of reducing free radical damage in the bodies of experimental animals:

1. Reduce calories in the diet to reduce the production of free radicals in metabolism.

2. Minimize dietary components such as copper and polyunsaturated fats which tend to increase free radical production.

3. Add to the diet one or more free radical quenchers such as vitamins E, C, A, B-1, B-5, B-6, zinc, selenium, BHT, and cysteine.

At age 78, Harman says he wants to live a bit longer, but he doesn't want to feel fatigued. "We will probably see an increase in life span with all the people who are now taking antioxidant supplements. I hope to be around a few more years to see it happen," he adds (Challem, 1995).



Application To Teaching: A Lesson on Antioxidant Nutrients

Do you remember the 1950 - 60s cartoon featuring a common house mouse (Mus musculus)? He lived in a cat-infested pharmacy with several other small rodents who struggled for their daily survival. One day, after a particularly brutal beating from the drug store cats, he ate a handful of vitamins and transformed his pointed snout, small upper-body, rounded ears, and long, hairless tail into a 'Mighty Mouse'. A modern-day corollary to the Mighty Mouse fable can be found in today's antioxidants - to the rescue!

1. Teaching about antioxidant nutrients can be enhanced by using the following focus activity. Rent a cartoon video with a scene from the television cartoon "Mighty Mouse" and show to the class. Choose a scene where Mighty Mouse transforms into a super-mouse by consuming nutrients/vitamins and ask the following questions:

   a. What factor was responsible for Mighty Mouse's super strength?

   b. What modern-day nutrients enable humans to increase muscular and cardiovascular strength and endurance?

2. Show a transparency of the levels of organization in nature starting with the subatomic particles that serve as the fundamental building blocks of all organisms. The hierarchy begins with subatomic particles (an electron, proton, or neutron; one of the three major particles of which atoms are composed); molecule (a unit of two or more atoms of the same or different elements bonded together); cell (the smallest living unit as part of a multicellular organism); tissue (a group of cells and intercellular substances functioning together in a specialized activity); organ (a structural unit in which tissues are combined in specific amounts to perform a common task); organ system (two or more organs interacting chemically and/or physically in ways that sustain life for the whole organism).

Application To Teaching: Continued

3. Explain to students that in order to understand how free radicals affect body organs and systems we must begin with the simplified model of atomic structure (show a transparency). The nucleus, a core region, consists of some number of protons and neutrons. Electrons spend as much time as possible near the nucleus and as far away from each other by moving in different orbitals, which are regions of space around the nucleus in which electrons are likely to be at any instant. Each orbital has enough room for two electrons, at most.

4. Explain to students that free radicals are atoms or groups of atoms that can cause damage to our cells, impairing our immune system and leading to infections and various degenerative diseases. Free radicals have lost one of the electrons that keep them chemically stable and in their frenetic search for a replacement, they'll steal one from another molecule, which in turn will steal another molecule's electron, etc... until the cycle is stopped by the body's antioxidants. In the process, free radicals damage DNA, proteins, lipids (implicated in heart disease), and carbohydrates, body tissues (linings of arteries), causing cell and tissue degeneration. Some of the diseases to which free radicals are thought to contribute are cancer, atherosclerosis, stroke, myocardial infarction, senile cataracts, Parkinson's disease, rheumatoid arthritis, and the aging process.

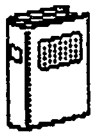
5. Free radicals are simply the waste products of ordinary metabolic processes, such as breathing and immune reactions. Thus, some oxidant activity eludes control and is beneficial to the body. But, the environmental free radicals are destructive; such as ionizing radiation, air pollutants, toxic industrial chemicals, pesticides, cigarette smoke, and drugs. Other sources of free radicals come from too vigorous exercise (marathon-type activities), over-heating cooking oils (deep-fat frying), consuming hydrogenated oils (potato chips, hydrogenated peanut butter and oils) eating ground red meats (hamburgers, sausage, hot dogs), overexposure to the sun's rays and chronic stress (Pearson & Shaw, 1982).

Application To Teaching: Continued

6. There are three known free radicals - the superoxide, the hydroxyl, and peroxide. The way in which these free radicals are normally kept in check is by the action of free-radical scavengers that occur naturally in the body. These scavengers neutralize the free radicals and certain enzymes serve this vital function. Four important enzymes that neutralize free radicals naturally are superoxide dismutase (SOD), methione reductase, catalase, and glutathione peroxidase.

7. Vitamins C, E, beta-carotene (a precursor of Vitamin A), gamma-linoleic acid (GLA), L-cysteine, L-glutathione, selenium, superoxide dismutase, and pycnogenol are all antioxidants that help protect the body from the formation of free radicals. If the diet is inadequate or lacking in the appropriate antioxidants, or if the system is overwhelmed by free radicals, you can take the above listed antioxidants to quench the free radical particles.

8. Ask students to make and share a brief list of all the fruits and vegetables that they have consumed in the past two days. Then ask; "What prevents you from including more fresh fruits and vegetables in your diet ?" This exercise typically is not a very difficult cognitive process as most high school and college students do not consume an adequate amount of these two food groups. A Cornell University study found that the more frequently people ages 13 to 21 ate away from home, the fewer nutrients they consumed (U.S. Dept. of Agriculture, 1984). The Department of Agriculture did a survey and found that on a given day 30 percent of elementary school children and about 60 percent of teenagers had eaten no fruit at all (Haas, 1993). An NCI study found that at least one in four children in elementary and high school does not even eat one serving of vegetables (not counting French Fries) per day (U.S. News and World Report, 1994). In addition, in 1992 the average American family spent 40 cents of every food dollar on snacks and meals eaten away from home, up from just 29 cents in 1970 (U.S.Dept. of Agriculture, 1985).



Application To Teaching: Continued

9. Explain to students that by simply eating fresh fruits and vegetables, deeper in color and unprocessed or heated, you can get a generous supply of disease-fitting antioxidants. The National Cancer Institute (NCI) urges all Americans to eat at least five servings of fruit and vegetables each day. One serving of a vegetable can be any one of the following amounts; 1/2 cup of chopped raw or cooked vegetables or 1 cup of leafy raw vegetables. One serving of fruit may be 1 piece of fruit or melon wedge, 3/4 cup of juice, 1/2 cup of canned fruit, or 1/4 cup of dried fruit. The U.S. Generally you get more antioxidants if you eat:

- red grapes rather than green or white grapes
- red and yellow onions instead of white onions
- cabbage, cauliflower and broccoli raw or lightly microwaved
- garlic raw and crushed
- extra virgin cold-pressed olive oil rather than commercially processed cooking oils
- deep, dark green leafy vegetables
- pink grapefruit rather than white grapefruit
- whole fruits rather than juices
- deep orange carrots, sweet potatoes and pumpkins

Exciting news is appearing almost every day in medical journals about the role of antioxidants in the prevention of diseases. Higher intakes of Vitamin E (100 to 800 units daily) is thought to prevent oxidation of LDL cholesterol and its absorption by blood vessels. Preliminary studies have shown a 37 to 40 percent reduction in the risk of heart disease in individuals taking 400 IU's of Vitamin E daily (Gey, 1991).

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