

Oxidative Stress in the Pathogenesis of Disease and Aging; Opportunity for Intervention

Preliminary Edition

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ABSTRACT

Normal metabolism produces free radical molecules. Oxidative stress is the imbalance between free radical production and the antioxidant cascade. This stress is associated with the pathogenesis of multiple disorders including cancer, stroke, coronary heart disease, cataracts, macular degeneration, depression and even the rate of aging. Nutrition includes the ingestion of physiologic doses of antioxidants from fruits, vegetables and grains. These phytochemicals in conjunction with endogenous antioxidants provide an interdependent network of buffers against free radical damage. Nutrition should not be confused with medication which is the ingestion of pharmacologic or unbalanced doses of components from herbal sources.

Free radical chemistry and molecular biology has given new insight into the pathogenesis of disease. Oxidative stress caused by free radical molecules results in damage to macromolecules that leads to disease and aging. Insight into this process will help physicians in their antioxidant nutritional advice to patients. This will provide the opportunity for prevention of disease and slow the rate of aging which will save billions of dollars and untold human misery. Many physicians do not recommend food supplements to patients or when they do it is often in the form of supplemental tablets of food extracts such as vitamin E, beta-carotene, folic acid, or ascorbic acid. These extracts are pharmacologic doses and by definition incomplete nutrition. The balance of nutrition that is needed can only be obtained from whole food. Normal metabolism produces large numbers of the free radicals (namely hydroxyl, hydrogen peroxide, and superoxide) that are the same as those produced by radiation. A typical rat cell produces twenty billion free radical molecules per day. The rat cell is metabolically seven times more active than a human cell but this still means humans generate one to three billion free radicals per day per cell. (1) Antioxidants neutralize free radicals and protect against such oxidative damage. Unless protected by antioxidants, macromolecules such as RNA, DNA, proteins, and lipids are damaged by these free radicals. The lipid damage occurs to circulating lipids, semipermeable membrane lipids and lipid components of such essential molecules as axonal sheaths of the central nervous system. Antioxidants are a complicated and interdependent cascade.² Some are endogenous which human tissue can make:

- Superoxide dismutase
- Glutathione peroxidase
- Glutathione S-transferases
- Catalase
- Proteases
- Glycosylases
- Ceruloplasmin
- Transferrin, ferritin
- Peroxisomes

Others are exogenous, we must eat them. These nutritional chemicals (phytochemicals) come from fruits, vegetables and grains. There are thousands of phytochemicals that are not designated as vitamins (since a deficiency disease hasn't been identified for them) that have an important role in human nutrition. The universal recommendation for three to five servings of vegetables and two to four servings of fruits per day has been made for over one hundred years, yet only 9% of Americans eat five servings per day. As antioxidants, phytochemicals are destroyed and must be replenished or reconstituted continuously. That is, we must eat them ever day.

AMERICAN NUTRITION

The magnitude of the problem is quite significant. Nutritional problems begin in childhood.^{3,4} Over ninety percent of American adults don't get five servings of fruits and vegetables per day. Foods that have been cooked, frozen, stored, micro-waved or irradiated may have had some damage to the phytochemical content. Radiation of foods

