OXIDATIVE STRESS AND FREE RADICAL DAMAGE TO SKIN

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FREE RADICAL THEORY OF AGING

The National Institutes of Health (NIH) recognizes 20–30 different theories of aging, the most widely accepted of which is the Free Radical Theory. This theory was first developed by Denham Harman and has been discussed for more than 50 years. The Free Radical Theory states that accumulated free radical damage and oxidative stress alter biochemical and cellular processes as aging damage accumulates. Most free radical damage occurs during times of active metabolic turnover. In humans, this occurs in early puberty for males and in pre-puberty and early puberty for females. Also during this time, humans possess the most physiologic reserve. However, as damage accumulates, our physiologic reserve becomes depleted. A 20-year-old faced with trauma or biochemical assault can accommodate and recover faster than an 80-year-old, whose physiologic reserve has been depleted.

A great deal of scientific evidence supports the Free Radical Theory. When more free radical damage occurs than can be neutralized by internal defenses, a state of oxidative stress exists. Living in stressful environments overwhelms the body's natural defenses against free radical damage. Ongoing oxidative stress directly relates to an increased rate of aging and eventual illness. Other biologic mechanisms such as inflammation, glycation, and DNA damage also play roles in the process of aging. But even these additional causes of aging are arguably related to or subsets of oxidative stress.

OXIDATIVE STRESS AND DISEASE

When a critical amount of oxidative stress occurs, "diseases of aging" can manifest as diabetes, atherosclerosis, strokes, or cancer. Many common diseases, such as infection, injury, or trauma, are the result of simple insult to the organism. Infection and trauma are not the results of aging but simply the risks of living in one's environment. As the average lifespan of humans has lengthened, there has been an increased frequency of age-related diseases associated with oxidative stress. These particular diseases occur in the older members of the population and are rarely seen in younger persons.

A recently discovered strain of yeast, found to age faster with better resistance to oxidative stress, has shed light on the enormous complexities of aging mechanisms. The yeast's ability to control oxidative stress may be related to a process called hormesis. Hormesis is a complicated internal process designed to help neutralize low levels of free radical formation by increasing other oxidative processes. All forms of oxidative stress may not be equal in their effects on aging, hence the yeast's successful employment of specific oxidative reactions to combat aging.

INFLAMMATION

Inflammation accompanies and potentiates free radical damage. As free radical damage occurs, cells and tissues are damaged. The body attempts to clear away damaged cells by activating various inflammatory pathways. Activated cells release assorted chemicals, triggering inflammation. Inflammation destroys and liquefies damaged tissue so it can be removed. However, inflammation is never restricted only to damaged cells, and it spills over into surrounding healthy tissue. Thus, inflammation, although designed to heal, might collaterally damage normal tissue.

SOURCES OF FREE RADICAL DAMAGE

Skin receives 80% of its free radical damage from exposure to the sun's rays. Solar rays are composed of packets of energy called photons, which are very high-energy particles—i.e. free radicals.

For tissues other than skin, more than 85% of all free radical damage comes from the cell's own metabolism. Our cells take oxygen inhaled by the lungs and use it in enzymatic reactions to burn fuel—glucose, fat, or even protein—and create energy. Each cell uses its energy to perform its own individual function. However, each cell makes extra energy. As energy is created, radicals are created. The extra radicals "spin off" as free radicals. These extra packets of energy are called free radicals because they are not committed to any particular ongoing biochemical reaction. Free radicals penetrate into the interior of the cell, combining with whatever structure they strike, damaging that structure.

The skin, being the body's first environmental defense, is exposed to other sources of free radical damage in addition to sun and internal cellular metabolism. Other sources of free radical damage to the skin include ozone, pollutants, applied substances (some sunscreens), alcohol, severe physical and emotional stress, poor nutrition, obesity, and toxins. Smoking is also critically damaging to cells and tissues, by delivering massive amounts of free radicals with every puff.

FREE RADICALS AND ANTIOXIDANTS

There are mechanisms for neutralizing free radicals, such as antioxidants. Antioxidants absorb free radicals and stop the negative cascade of molecular damage. There are lipid-soluble antioxidants, such as vitamin E, which target the lipid-rich or fat-containing parts of cells. There are aqueous antioxidants, such as vitamin C, which protect the water-containing fluid portions of cells. Extrinsic antioxidants are ingested or applied topically, whereas intrinsic antioxidants are present inside cells and are synthesized by the body. Intrinsic antioxidants include enzymes like superoxide dismutase (SOD), catalase, and glutathione peroxidase. These enzymes are manufactured within the interior of the cell, as an inherent defense against free radical damage.

A condition of oxidative stress occurs when more free radicals exist than can be neutralized by all antioxidants combined. Humans are always in states of oxidative stress. There are always excess free radicals causing damage and the slow decline of the body, and this translates to a natural process of aging. For skin, the most effective strategy to combat oxidative stress is to avoid sun exposure, use sunscreen, and apply a combination of topical antioxidants.

FREE RADICAL DAMAGE CASCADE

The abbreviated chemical reactions below illustrate the accumulation of free radical damage and oxidative stress. The free radical O* contains very high energy and combines with the first molecule it touches. In combining with this structure, O* damages it, and in the process, another free radical is created. The second free radical then combines with the first structure it touches. The negative cascade continues until the free radicals are neutralized. For this reason, antioxidants are crucial to maintaining cellular function as we age.

- O* + cell membrane → damaged cell membrane + A* (Cell membrane protects integrity of cell)
- A* + mitochondria → damaged mitochondria + B* (Mitochondria produce energy for the cell)
- B* + DNA → damaged DNA + D* (DNA is the genetic mechanism of the cell that directs all cellular function and reproduces itself to create another cell. Damaged DNA leads to a cancerous or malignant cell)
- D* + cellular protein/collagen/elastin → → damaged elastic tissue (wrinkles) + E*

The free radical damage cascade shown above depends upon the unpaired electron in the free radical's outer orbit, which captures an electron from other molecules, creating more free radicals in this process and causing ongoing collateral damage. The beauty of antioxidants is that they serve as electron donors to free radicals, thus neutralizing the free radicals but remaining stable themselves. Antioxidants stop the ongoing cascade of perpetual free radical creation and minimize collateral damage.

Skin cells, being near the surface of the body, are bombarded with additional stressors from the environment that fail to reach other cells deep within the body's interior. This increases the volume of oxidative stress present in the skin. Once a free radical touches the cell, the cascade of free radical damage begins, as illustrated in the above reactions.

Antioxidants can neutralize free radicals before they touch the cell, as well as stop ongoing interior cellular damage. Antioxidants stop the cascade of free radical damage by donating an electron, thus ending the cycle of further free radical creation. It is important to have antioxidant protection at all cellular layers, because it is impossible to stop all free radicals at the surface. Many of them get through the initial skin barrier or come from inside the cell itself via cellular metabolism. Antioxidants combining with free radicals "upstream" can help to prevent a large cascade of damage. In this way, antioxidants can prevent the multiplication of damage seen "downstream."

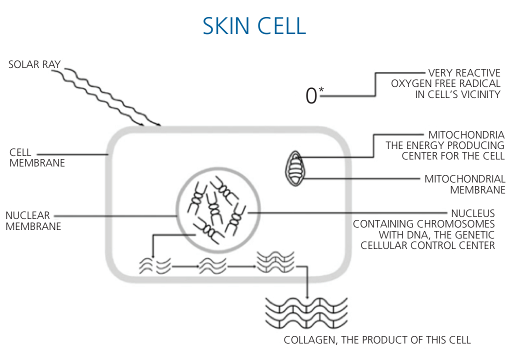

Figure 3. Skin cell diagram illustrating impact of free radical damage, which can occur at all structure levels.

CELL STRUCTURE AND OXIDATIVE STRESS

Membranes are lipid-soluble barriers designed to enclose cells and also interior organelles such as the mitochondria and nucleolus. If they become damaged, they have difficulty protecting their interior structures, as well as letting the right substances in while keeping other substances out. Lipid-soluble antioxidants like vitamin E protect cell membranes and other lipid structures.

Interior cellular structures and interstitial fluid between cells contain mostly water. Therefore, aqueous or water-soluble antioxidants like vitamin C protect these areas from free radical damage.

DNA directs cell function and regulates cellular reproduction. In the case of skin, the function of one cell type might be to make collagen. If the DNA is damaged, it may direct the formation of collagen containing mistakes. Biochemically inaccurate collagen would be unable to function properly. Impaired collagen might have poor elasticity, causing wrinkles, or be unable to bind with other collagen chains, causing wrinkles, loss of resilience, and improper scarring. If enough DNA damage occurs, the cell can become malignant—i.e. cancerous.

Damaged mitochondria are unable to produce adequate energy for the cell. A specific amount of energy is required for the cell to function. Damaged mitochondria may produce too little or too much energy, contributing to an increase in free radical damage.

TYPES OF ANTIOXIDANTS

Antioxidants can be ingested (taken orally) or applied topically to the skin. As little as 1% of antioxidants taken orally reach the surface of the skin. To maximize antioxidant protection, it is necessary to apply effective topical antioxidants to the skin.

Effective topical antioxidants must be high-quality, stable, and in the purest form. Since skin's primary function is to keep some substances in and other environmental agents out, the design of topical antioxidants becomes particularly challenging. Successfully formulated topical antioxidants penetrate the outermost barriers and reach the interior of the cell.

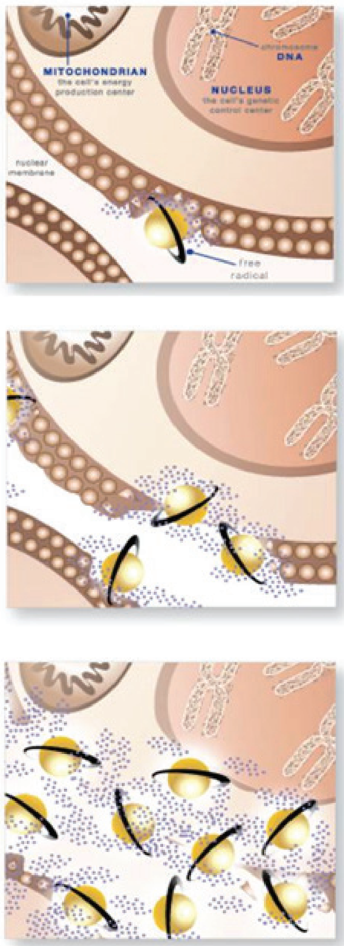

Figure 2. Illustration of a free radical damage cascade with ongoing electron theft and perpetual free radical creation. This results in an ever-widening circle of structural damage and further free radical creation.

Suggested Products—All iS CLINICAL® and iS products are helpful for oxidative stress and free radical damage.

ANTIOXIDANTS

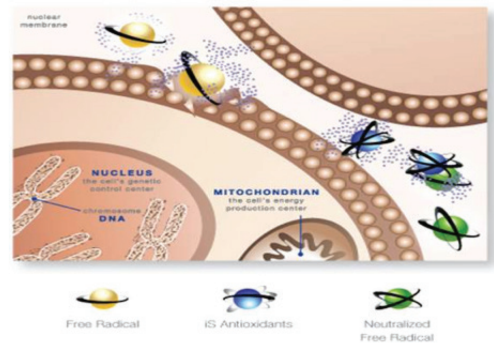

Figure 3. Antioxidants neutralize free radicals by donating an electron, thus stopping the ongoing cascade of damage and further creation of free radicals.

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